```
FILE 'HOME' ENTERED AT 12:42:20 ON 05 JUN 2003

=> index bioscience medicine meetings
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
      BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
      CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
      DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 12:42:34 ON 05 JUN 2003

79 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s RICIN AND (PROTEASE? OR PROTEINASE?) AND CLEAV? AND (RECOMBINANT OR FUSION)
          3   FILE ADISINSIGHT
          5   FILE BIOSIS
          6   FILE BIOTECHABS
          6   FILE BIOTECHDS
          2   FILE BIOTECHNO
          1   FILE CANCERLIT
         15   FILE CAPLUS
        245   FILE DGENE
  24 FILES SEARCHED...
          1   FILE EMBAL
          2   FILE EMBASE
          1   FILE ESBIOBASE
          1   FILE GENBANK
         12   FILE IFIPAT
          4   FILE MEDLINE
          1   FILE PASCAL
  54 FILES SEARCHED...
          2   FILE PROMT
          9   FILE SCISEARCH
         13   FILE TOXCENTER
       2858   FILE USPATFULL
         33   FILE USPAT2
          8   FILE WPIDS
          8   FILE WPINDEX
          1   FILE NLDB

  23 FILES HAVE ONE OR MORE ANSWERS,    79 FILES SEARCHED IN STNINDEX

L1   QUE RICIN AND (PROTEASE? OR PROTEINASE?) AND CLEAV? AND (RECOMBINANT OR FU
       SION)

=> file hits
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         2.20       2.41

FILE 'USPATFULL' ENTERED AT 12:45:02 ON 05 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'DGENE' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'USPAT2' ENTERED AT 12:45:02 ON 05 JUN 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'CAPLUS' ENTERED AT 12:45:02 ON 05 JUN 2003
```

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 ACS

FILE 'IFIPAT' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 IFI CLAIMS(R) Patent Services (IFI)

FILE 'SCISEARCH' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'WPIDS' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'WPINDEX' ACCESS NOT AUTHORIZED

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'BIOTECHDS' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 THOMSON DERWENT AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'BIOSIS' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 12:45:02 ON 05 JUN 2003

FILE 'ADISINSIGHT' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Adis Data Information BV

FILE 'BIOTECHNO' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'EMBASE' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'PROMT' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Gale Group. All rights reserved.

FILE 'CANCERLIT' ENTERED AT 12:45:02 ON 05 JUN 2003

FILE 'EMBAL' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'ESBIOBASE' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'GENBANK' ENTERED AT 12:45:02 ON 05 JUN 2003

FILE 'PASCAL' ENTERED AT 12:45:02 ON 05 JUN 2003
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2003 INIST-CNRS. All rights reserved.

FILE 'NLDB' ENTERED AT 12:45:02 ON 05 JUN 2003
COPYRIGHT (C) 2003 Gale Group. All rights reserved.

=> s l1
L2 2858 FILE USPATFULL
L3 245 FILE DGENE
L4 33 FILE USPAT2
L5 15 FILE CAPLUS
L6 13 FILE TOXCENTER

```
L7          12 FILE IFIPAT
L8           9 FILE SCISEARCH
L9           8 FILE WPIDS
L10          6 FILE BIOTECHDS
L11          5 FILE BIOSIS
L12          4 FILE MEDLINE
L13          3 FILE ADISINSIGHT
L14          2 FILE BIOTECHNO
L15          2 FILE EMBASE
L16          2 FILE PROMT
L17          1 FILE CANCERLIT
L18          1 FILE EMBAL
L19          1 FILE ESBIOBASE
L20          1 FILE GENBANK
L21          1 FILE PASCAL
L22          1 FILE NLDB

TOTAL FOR ALL FILES
L23       3223 L1

=> s RICIN (s) (PROTEASE? OR PROTEINASE?) (s) CLEAV? and RECOMBINANT
L24         48 FILE USPATFULL
L25        245 FILE DGENE
L26          0 FILE USPAT2
L27          1 FILE CAPLUS
L28          0 FILE TOXCENTER
L29          2 FILE IFIPAT
L30          4 FILE SCISEARCH
L31          4 FILE WPIDS
L32          3 FILE BIOTECHDS
L33          4 FILE BIOSIS
L34          0 FILE MEDLINE
L35          3 FILE ADISINSIGHT
L36          1 FILE BIOTECHNO
L37          1 FILE EMBASE
L38          0 FILE PROMT
L39          1 FILE CANCERLIT
L40          0 FILE EMBAL
L41          0 FILE ESBIOBASE
L42          0 FILE GENBANK
L43          0 FILE PASCAL
L44          0 FILE NLDB

TOTAL FOR ALL FILES
L45        317 RICIN (S) (PROTEASE? OR PROTEINASE?) (S) CLEAV? AND RECOMBINANT

=> dup rem l45
DUPLICATE IS NOT AVAILABLE IN 'DGENE, ADISINSIGHT, GENBANK'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L45
L46         306 DUP REM L45 (11 DUPLICATES REMOVED)

=> s l45 and metalloproteinase
L47          1 FILE USPATFULL
L48         73 FILE DGENE
L49          0 FILE USPAT2
L50          0 FILE CAPLUS
L51          0 FILE TOXCENTER
L52          0 FILE IFIPAT
L53          0 FILE SCISEARCH
L54          0 FILE WPIDS
L55          0 FILE BIOTECHDS
L56          0 FILE BIOSIS
L57          0 FILE MEDLINE
L58          3 FILE ADISINSIGHT
```

```
L59           0 FILE BIOTECHNO
L60           0 FILE EMBASE
L61           0 FILE PROMT
L62           0 FILE CANCERLIT
L63           0 FILE EMBAL
L64           0 FILE ESBIOBASE
L65           0 FILE GENBANK
L66           0 FILE PASCAL
L67           0 FILE NLDB

TOTAL FOR ALL FILES
L68          77 L45 AND METALLOPROTEINASE

=> dup rem l68
DUPLICATE IS NOT AVAILABLE IN 'DGENE, ADISINSIGHT, GENBANK'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L68
L69           77 DUP REM L68 (0 DUPLICATES REMOVED)

=> d l69 1-77 ibib abs
NO VALID FORMATS ENTERED FOR FILE 'ADISINSIGHT'
In a multifile environment, each file must have at least one valid
format requested.  Refer to file specific help messages or the
STNGUIDE file for information on formats available in individual
files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):so au ti abs

L69  ANSWER 1 OF 77  USPATFULL
IN      Benson, Darin R., Seattle, WA, UNITED STATES
        Kalos, Michael D., Seattle, WA, UNITED STATES
        Lodes, Michael J., Seattle, WA, UNITED STATES
        Persing, David H., Redmond, WA, UNITED STATES
        Hepler, William T., Seattle, WA, UNITED STATES
        Jiang, Yuqiu, Kent, WA, UNITED STATES
TI      Compositions and methods for the therapy and diagnosis of pancreatic
        cancer
AB      Compositions and methods for the therapy and diagnosis of cancer,
        particularly pancreatic cancer, are disclosed. Illustrative compositions
        comprise one or more pancreatic tumor polypeptides, immunogenic portions
        thereof, polynucleotides that encode such polypeptides, antigen
        presenting cell that expresses such polypeptides, and T cells that are
        specific for cells expressing such polypeptides. The disclosed
        compositions are useful, for example, in the diagnosis, prevention
        and/or treatment of diseases, particularly pancreatic cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L69   ANSWER 2 OF 77  DGENE (C) 2003 THOMSON DERWENT
IN    Braun C; Purac A; Borgford T
TI    New proteins comprising A and B chains of ricin-like toxin
      linked by a novel linker sequence that is specifically cleaved
      and activated by protease specific to cancer is useful for
      treating inflammation and cancer  -
AN    AAG66985  Peptide       DGENE
AB    The invention relates to a recombinant protein comprising an A
      chain of a ricin-like toxin, a B chain of a ricin
      -like toxin and a heterologous linker that links the A and B chains. The
      linker sequence contains a cleavage recognition site for a
      specific protease such as those found in inflammatory cells and
      cancer cells. The protein is useful for inhibiting or destroying cells
      expressing a specific protease, e.g. cancer cells found in T-
      and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic
      cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal
      cancer, breast cancer, prostate cancer or non-small cell lung cancer, or
      cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or
```

SO Adis R&D Insight

=> d l69 1-77 ibib abs
NO VALID FORMATS ENTERED FOR FILE 'ADISINSIGHT'
In a multifile environment, each file must have at least one valid format requested. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): au so ti abs bib

L69 ANSWER 1 OF 77 USPATFULL
IN Benson, Darin R., Seattle, WA, UNITED STATES
Kalos, Michael D., Seattle, WA, UNITED STATES
Lodes, Michael J., Seattle, WA, UNITED STATES
Persing, David H., Redmond, WA, UNITED STATES
Hepler, William T., Seattle, WA, UNITED STATES
Jiang, Yuqiu, Kent, WA, UNITED STATES
TI Compositions and methods for the therapy and diagnosis of pancreatic cancer
AB Compositions and methods for the therapy and diagnosis of cancer, particularly pancreatic cancer, are disclosed. Illustrative compositions comprise one or more pancreatic tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly pancreatic cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:106233 USPATFULL
TI Compositions and methods for the therapy and diagnosis of pancreatic cancer
IN Benson, Darin R., Seattle, WA, UNITED STATES
Kalos, Michael D., Seattle, WA, UNITED STATES
Lodes, Michael J., Seattle, WA, UNITED STATES
Persing, David H., Redmond, WA, UNITED STATES
Hepler, William T., Seattle, WA, UNITED STATES
Jiang, Yuqiu, Kent, WA, UNITED STATES
PA Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PI US 2003073144 A1 20030417
AI US 2002-60036 A1 20020130 (10)
PRAI US 2001-333626P 20011127 (60)
US 2001-305484P 20010712 (60)
US 2001-265305P 20010130 (60)
US 2001-267568P 20010209 (60)
US 2001-313999P 20010820 (60)
US 2001-291631P 20010516 (60)
US 2001-287112P 20010428 (60)
US 2001-278651P 20010321 (60)
US 2001-265682P 20010131 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 14253
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L69 ANSWER 2 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66985 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66985 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP325 (MMP-9).

L69 ANSWER 3 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66984 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66984 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP324 (MMP-9).

L69 ANSWER 4 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66983 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66983 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP323 (MMP-9).

L69 ANSWER 5 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66982 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A

chain of a **ricin**-like toxin, a B chain of a **ricin**
-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66982 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP322 (UPA).

L69 ANSWER 6 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66981 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**
-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66981 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP321 (UPA).

L69 ANSWER 7 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66980 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66980 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP320 (UPA).

L69 ANSWER 8 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66979 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and

cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66979 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP318 (MMP-9).

L69 ANSWER 9 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66978 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66978 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP316 (MMP-9).

L69 ANSWER 10 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66977 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66977 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP315 (UPA).

L69 ANSWER 11 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66976 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal

cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66976 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP314 (UPA).

L69 ANSWER 12 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66975 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66975 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English

OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP313 (UPA).

L69 ANSWER 13 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66974 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66974 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP309 (MMP-9).

L69 ANSWER 14 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66973 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain

a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66973 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP308 (MMP-9).

L69 ANSWER 15 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66972 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66972 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP305 (MMP-9).

L69 ANSWER 16 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66971 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66971 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP304 (MMP-9).

L69 ANSWER 17 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66970 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a

cleavage recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66970 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP303 (MMP-9).

L69 ANSWER 18 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66969 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAG66969 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP302 (MMP-9).

L69 ANSWER 19 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
AN AAG66968 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAG66968 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP301 (MMP-9).

L69 ANSWER 20 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66967 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is the wild type preproricin linker sequence.
AN AAG66967 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant wild type ricin linker peptide.

L69 ANSWER 21 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79940 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79940 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP325 MMP-9 variant linker region DNA.

L69 ANSWER 22 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79939 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and

cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79939 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 325-5'.

L69 ANSWER 23 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79938 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79938 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 325-3'.

L69 ANSWER 24 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79936 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79936 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP324 MMP-9 variant linker region DNA.

L69 ANSWER 25 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79935 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain

a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79935 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 324-5'.

L69 ANSWER 26 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79934 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79934 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 324-3'.

L69 ANSWER 27 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
AN AAI79932 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79932 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP323 MMP-9 variant linker region DNA.

L69 ANSWER 28 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79931 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79931 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 323-5'.

L69 ANSWER 29 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79930 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79930 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 323-3'.

L69 ANSWER 30 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79928 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells

expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79928 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP322 UPA variant linker region DNA.

L69 ANSWER 31 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79927 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79927 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 322-5'.

L69 ANSWER 32 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79926 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79926 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 322-3'.

L69 ANSWER 33 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79924 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders

and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79924 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP321 UPA variant linker region DNA.

L69 ANSWER 34 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79923 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79923 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 321-5'.

L69 ANSWER 35 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79922 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79922 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 321-3'.

L69 ANSWER 36 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79920 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79920 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP320 UPA variant linker region DNA.

L69 ANSWER 37 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79919 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79919 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 320-5'.

L69 ANSWER 38 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79918 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and

cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79918 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 320-3'.

L69 ANSWER 39 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79916 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79916 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP318 MMP-9 variant linker region DNA.

L69 ANSWER 40 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79915 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79915 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 318-5'.

L69 ANSWER 41 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79914 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain

a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79914 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 318-3'.

L69 ANSWER 42 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79912 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79912 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP316 MMP-9 variant linker region DNA.

L69 ANSWER 43 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin

linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79911 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79911 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 316-5'.

L69 ANSWER 44 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79910 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79910 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 316-3'.

L69 ANSWER 45 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79908 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79908 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP315 UPA variant linker region DNA.

L69 ANSWER 46 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79907 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a

specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79907 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 315-5'.

L69 ANSWER 47 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79906 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79906 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 315-3'.

L69 ANSWER 48 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79904 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79904 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP314 UPA variant linker region DNA.

L69 ANSWER 49 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79903 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer

and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79903 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 314-5'.

L69 ANSWER 50 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79902 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79902 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 314-3'.

L69 ANSWER 51 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79900 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79900 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP313 UPA variant linker region DNA.

L69 ANSWER 52 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79899 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79899 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 313-5'.

L69 ANSWER 53 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79898 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79898 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 313-3'.

L69 ANSWER 54 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79896 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and

cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79896 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP309 MMP-9 variant linker region DNA.

L69 ANSWER 55 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79895 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79895 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 309-5'.

L69 ANSWER 56 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79894 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79894 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 309-3'.

L69 ANSWER 57 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79891 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain

a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79891 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP308 MMP-9 variant linker region DNA.

L69 ANSWER 58 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79890 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79890 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 308-5'.

L69 ANSWER 59 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin

linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79889 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79889 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 308-3'.

L69 ANSWER 60 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79887 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79887 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin

linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP305 MMP-9 variant linker region DNA.

L69 ANSWER 61 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79886 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79886 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 305-5'.

L69 ANSWER 62 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79885 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a

specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79885 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 305-3'.

L69 ANSWER 63 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79883 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79883 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004

US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP304 MMP-9 variant linker region DNA.

L69 ANSWER 64 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79882 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79882 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 304-5'.

L69 ANSWER 65 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79881 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer

and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79881 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 304-3'.

L69 ANSWER 66 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79879 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.

AN AAI79879 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP303 MMP-9 variant linker region DNA.

L69 ANSWER 67 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79878 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79878 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 303-5'.

L69 ANSWER 68 OF 77 DGENE (C) 2003 THOMSON DERWENT

IN Braun C; Purac A; Borgford T

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79877 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79877 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 303-3'.

L69 ANSWER 69 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79875 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79875 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP302 MMP-9 variant linker region DNA.

L69 ANSWER 70 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79874 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The

linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79874 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 302-5'.

L69 ANSWER 71 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79873 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79873 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 302-3'.

L69 ANSWER 72 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79871 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix **metalloproteinase** 9 (MMP-9) or UPA.
AN AAI79871 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP301 MMP-9 variant linker region DNA.

L69 ANSWER 73 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79870 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or

central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79870 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 301-5'.

L69 ANSWER 74 OF 77 DGENE (C) 2003 THOMSON DERWENT
IN Braun C; Purac A; Borgford T
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79869 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79869 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 301-3'.

L69 ANSWER 75 OF 77 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

L69 ANSWER 76 OF 77 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

L69 ANSWER 77 OF 77 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

=>

=> d l46 1-306 ibib abs
NO VALID FORMATS ENTERED FOR FILE 'ADISINSIGHT'
In a multifile environment, each file must have at least one valid
format requested. Refer to file specific help messages or the
STNGUIDE file for information on formats available in individual
files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):so ti abs bib au

L46 ANSWER 1 OF 306 USPATFULL DUPLICATE 1
TI Antiviral ricin-like proteins
AB The present invention provides a protein having an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker amino acid sequence, linking the A and B chains. The linker sequence contains a **cleavage** recognition site for a retroviral **protease** such as HIV or an HTLV **protease**. The invention also relates to a nucleic acid molecule encoding the protein and to expression vectors incorporating the nucleic acid molecule. Also provided is a method of inhibiting or destroying mammalian cells infected with a retrovirus utilizing the proteins of the invention; and pharmaceutical compositions for treating HIV infections and human T-cell leukemias involving HTLV.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:67556 USPATFULL
TI Antiviral ricin-like proteins
IN Borgford, Thor, Burnaby, CANADA
PA Twinstrand Therapeutics Inc., Vancouver, CANADA (non-U.S. corporation)
PI US 6531125 B1 20030311
AI US 2000-550117 20000414 (9)
RLI Continuation-in-part of Ser. No. US 1999-147208, filed on 2 Mar 1999, now patented, Pat. No. US 6333303
DT Utility
FS GRANTED
EXNAM Primary Examiner: Stucker, Jeffrey
LREP Bereskin & Parr, Gravelle, Micheline
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 47 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 2702
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Borgford, Thor, Burnaby, CANADA

L46 ANSWER 2 OF 306 USPATFULL
TI Feline immunodeficiency virus gene therapy vectors
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency virus, as well as related packaging cell lines, methods for production, and methods of use.

AN 2003:152945 USPATFULL
TI Feline immunodeficiency virus gene therapy vectors
IN Johnston, Julie C., Wilmington, DE, UNITED STATES
Sauter, Sybille L., Del Mar, CA, UNITED STATES
Hsu, David Chi-Tang, San Diego, CA, UNITED STATES
Sheridan, Philip Lee, San Diego, CA, UNITED STATES
Hardy, Stephen F., San Francisco, CA, UNITED STATES
Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Yee, Jiing-Kuan, Del Mar, CA, UNITED STATES
PI US 2003104611 A1 20030605
AI US 2001-872696 A1 20010601 (9)
RLI Continuation of Ser. No. US 1999-231235, filed on 15 Jan 1999, PENDING
PRAI US 1998-71731P 19980116 (60)
US 1998-86825P 19980526 (60)
US 1999-114955P 19990104 (60)
DT Utility
FS APPLICATION

LREP CHIRON CORPORATION, Intellectual Property, P.O. Box 8097, Emeryville, CA, 94662-8097
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 5553
IN Johnston, Julie C., Wilmington, DE, UNITED STATES
Sauter, Sybille L., Del Mar, CA, UNITED STATES
Hsu, David Chi-Tang, San Diego, CA, UNITED STATES
Sheridan, Philip Lee, San Diego, CA, UNITED STATES
Hardy, Stephen F., San Francisco, CA, UNITED STATES
Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Yee, Jiing-Kuan, Del Mar, CA, UNITED STATES

L46 ANSWER 3 OF 306 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
AB Isolated nucleic acid molecules are disclosed, comprising an alphavirus nonstructural protein gene which, when operably incorporated into a **recombinant** alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

AN 2003:140556 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
IN Schlesinger, Sondra, St.Louis, MO, UNITED STATES
Frolov, IIya, St.Louis, MO, UNITED STATES
Dubenssky, Thomas W., JR., Delmar, CA, UNITED STATES
Polo, John M., Encinitas, CA, UNITED STATES
Belli, Barbara A., San Diego, CA, UNITED STATES
Dryga, Sergev A., Fort Collins, CO, UNITED STATES
PI US 2003096397 A1 20030522
AI US 2000-507362 A1 20000218 (9)
RLI Division of Ser. No. US 1997-944465, filed on 6 Oct 1997, PENDING Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, ABANDONED Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, ABANDONED Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, ABANDONED Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, ABANDONED
DT Utility
FS APPLICATION
LREP Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA, 94662-8097
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 63 Drawing Page(s)
LN.CNT 8169
IN Schlesinger, Sondra, St.Louis, MO, UNITED STATES
Frolov, IIya, St.Louis, MO, UNITED STATES
Dubenssky, Thomas W., JR., Delmar, CA, UNITED STATES
Polo, John M., Encinitas, CA, UNITED STATES
Belli, Barbara A., San Diego, CA, UNITED STATES
Dryga, Sergev A., Fort Collins, CO, UNITED STATES

L46 ANSWER 4 OF 306 USPATFULL
TI Compositions and methods for the therapy and diagnosis of pancreatic cancer
AB Compositions and methods for the therapy and diagnosis of cancer, particularly pancreatic cancer, are disclosed. Illustrative compositions

comprise one or more pancreatic tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly pancreatic cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:106233 USPATFULL
TI Compositions and methods for the therapy and diagnosis of pancreatic cancer
IN Benson, Darin R., Seattle, WA, UNITED STATES
Kalos, Michael D., Seattle, WA, UNITED STATES
Lodes, Michael J., Seattle, WA, UNITED STATES
Persing, David H., Redmond, WA, UNITED STATES
Hepler, William T., Seattle, WA, UNITED STATES
Jiang, Yuqiu, Kent, WA, UNITED STATES
PA Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PI US 2003073144 A1 20030417
AI US 2002-60036 A1 20020130 (10)
PRAI US 2001-333626P 20011127 (60)
US 2001-305484P 20010712 (60)
US 2001-265305P 20010130 (60)
US 2001-267568P 20010209 (60)
US 2001-313999P 20010820 (60)
US 2001-291631P 20010516 (60)
US 2001-287112P 20010428 (60)
US 2001-278651P 20010321 (60)
US 2001-265682P 20010131 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 14253
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Benson, Darin R., Seattle, WA, UNITED STATES
Kalos, Michael D., Seattle, WA, UNITED STATES
Lodes, Michael J., Seattle, WA, UNITED STATES
Persing, David H., Redmond, WA, UNITED STATES
Hepler, William T., Seattle, WA, UNITED STATES
Jiang, Yuqiu, Kent, WA, UNITED STATES

L46 ANSWER 5 OF 306 USPATFULL
TI Anti-pathogen system and methods of use thereof
AB The present invention provides an anti-pathogen system comprising one or more fusion proteins that includes a transduction domain and a cytotoxic domain. The cytotoxic domain is specifically activated by a pathogen infection. The anti-pathogen system effectively kills or injures cells infected by one or a combination of different pathogens. Further provided are protein transduction domains that provide enhanced transduction efficiency.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:78080 USPATFULL
TI Anti-pathogen system and methods of use thereof
IN Dowdy, Steven F., Clayton, MO, UNITED STATES
PA Washington University (U.S. corporation)
PI US 2003054000 A1 20030320
AI US 2001-775052 A1 20010201 (9)
PRAI US 1998-82402P 19980420 (60)
US 1997-69012P 19971210 (60)
DT Utility

FS APPLICATION
LREP Dike, Bronstein, Roberts & Cushman, Intellectual Property Practice Group, EDWARDS & ANGELL, P.O. Box 9169, Boston, MA, 02209
CLMN Number of Claims: 86
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 3366
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dowdy, Steven F., Clayton, MO, UNITED STATES

L46 ANSWER 6 OF 306 USPATFULL
TI Functional lentiviral vector from an MLV-based backbone
AB Disclosed are gene therapy vectors based on chimeric murine leukemia virus-feline immunodeficiency virus gene therapy vectors which are suitable for a wide variety of gene therapy applications. Also disclosed are related packaging cell lines, methods for production, and methods of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:3530 USPATFULL
TI Functional lentiviral vector from an MLV-based backbone
IN Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Gasmi, Mehdi, San Diego, CA, UNITED STATES
Sauter, Sybille, Del Mar, CA, UNITED STATES
PI US 2003003565 A1 20030102
AI US 2001-996073 A1 20011127 (9)
PRAI US 2000-253419P 20001127 (60)
DT Utility
FS APPLICATION
LREP CHIRON CORPORATION, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA, 94662-8097
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 3778
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Gasmi, Mehdi, San Diego, CA, UNITED STATES
Sauter, Sybille, Del Mar, CA, UNITED STATES

L46 ANSWER 7 OF 306 USPATFULL
TI Producer cell that generates adenoviral vectors encoding a cytokine and a conditionally lethal gene
AB The present invention provides **recombinant** viral vectors carrying a vector construct which directs the expression of a gene product (e.g., HSVTK) that activates a compound with little or no cytotoxicity into a toxic product. Also provided are methods of destroying or inhibiting pathogenic agents in a warm blooded animal, comprising the step of administering to the animal a viral vector such as that described above, in order to inhibit or destroy the pathogenic agent.

AN 2003:142966 USPATFULL
TI Producer cell that generates adenoviral vectors encoding a cytokine and a conditionally lethal gene
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6569679 B1 20030527
AI US 1995-471645 19950606 (8)
RLI Division of Ser. No. US 1993-155944, filed on 18 Nov 1993, now abandoned Continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned Continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned Continuation-in-part of Ser. No. US

1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Guzo, David; Assistant Examiner: Leffers, Jr., Gerald G.
LREP Pochopien, Donald J., Harbin, Alisa A., Blackburn, Robert P.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 30 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 2735
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States

L46 ANSWER 8 OF 306 USPATFULL
TI Adenoviral vectors encoding a cytokine and a conditionally lethal gene
AB The present invention provides **recombinant** viral vectors carrying a vector construct which directs the expression of a gene product (eg. HSVTK) that activates a compound with little or no cytotoxicity into a toxic product. Also provided are methods of destroying or inhibiting pathogenic agents in a warm blooded animal, comprising the step of administering to the animal a viral vector such as that described above, in order to inhibit or destroy the pathogenic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2003:67673 USPATFULL
TI Adenoviral vectors encoding a cytokine and a conditionally lethal gene
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6531307 B1 20030311
AI US 1995-455014 19950531 (8)
RLI Division of Ser. No. US 1993-155944, filed on 18 Nov 1993, now abandoned Continuation-in-part of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned Continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Guzo, David; Assistant Examiner: Leffers, Jr., Gerald G.
LREP Pochopien, Donald, Harbin, Alisa A., Blackburn, Robert P.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 30 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 2673
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States

L46 ANSWER 9 OF 306 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 2
TI New promoter of a NTR1 gene or a JMT gene encoding jasmonic acid carboxyl methyltransferase, for inducing expression of a target gene in a plant, including therapeutic genes for use in humans or genes for constructing transgenic plants.
AN 2002-706996 [76] WPIDS
AB WO 200268644 A UPAB: 20021125
NOVELTY - A promoter of a NTR1 gene encoding jasmonic acid carboxyl methyltransferase cloned from Brassica campestris, or a promoter of a JMT gene encoding jasmonic acid carboxyl methyltransferase cloned from Arabidopsis sp., which induces expression of a target gene in a plant in response to an external stimulus, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following:

(1) a **recombinant** vector for plant transformation in which a promoter having a 4424 (S1) or 5290 (S2) sequence, given in the specification is linked to a target gene encoding a target protein, where the promoter is employed as an inducible promoter that induces expression of the target gene in response to an external stimulus;

(2) an Escherichia coli transformed with pBNTR1 or pBJMT, the **recombinant** vector of (1) with accession numbers KCTC 0966BP and KCTC 0967BP, respectively;

(3) a transgenic plant transformed with the **recombinant** vector; and

(4) a method for producing a target protein in a plant, comprising:

(a) constructing a **recombinant** vector for plant transformation in which a promoter having a nucleotide sequence of S1 or S2 is linked to a target gene encoding a target protein;

(b) transforming the plant with the **recombinant** vector for plant transformation; and

(c) inducing the promoter to express the target gene encoding the target protein by applying an external stimulus to the plant producing the target protein in the plant.

USE - The promoters are useful for inducing expression of a target gene, including therapeutic genes for use in humans, genes for constructing transgenic plants, or genes involved in the biosynthesis of useful metabolites, in a plant in response to external stimuli. The promoters are also useful for producing target proteins in a plant.

Dwg.0/13

AN 2002-706996 [76] WPIDS
DNC C2002-200573
TI New promoter of a NTR1 gene or a JMT gene encoding jasmonic acid carboxyl methyltransferase, for inducing expression of a target gene in a plant, including therapeutic genes for use in humans or genes for constructing transgenic plants.
DC B04 C06 D16
IN CHOI, G S; CHOI, Y D; JUNG, J J; KIM, J G; LEE, J S; LIM, J Y; PARK, M Y; SEO, H S; XUE, R; CHEONG, J; CHOI, K; CHOI, Y; KIM, J; LEE, J; LIM, J; PARK, M; SEO, H
PA (CHOI-I) CHOI Y D; (SCIG-N) SCIGEN HARVEST CO LTD; (CHOI-I) CHOI Y
CYC 100
PI WO 2002068644 A1 20020906 (200276)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
KR 2002069340 A 20020830 (200309)
ADT WO 2002068644 A1 WO 2002-KR307 20020225; KR 2002069340 A KR 2002-10015 20020225
PRAI KR 2001-9525 20010224
IN CHOI, G S; CHOI, Y D; JUNG, J J; KIM, J G; LEE, J S; LIM, J Y; PARK, M Y; SEO, H S; XUE, R; CHEONG, J; CHOI, K; CHOI, Y; KIM, J; LEE, J; LIM, J; PARK, M; SEO, H

L46 ANSWER 10 OF 306 USPATFULL
TI Compositions and methods for the therapy and diagnosis of colon cancer
AB Compositions and methods for the therapy and diagnosis of cancer, particularly colon cancer, are disclosed. Illustrative compositions comprise one or more colon tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly colon cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 2002:272801 USPATFULL
TI Compositions and methods for the therapy and diagnosis of colon cancer
IN Stolk, John A., Bothell, WA, UNITED STATES
Xu, Jiangchun, Bellevue, WA, UNITED STATES
Chenault, Ruth A., Seattle, WA, UNITED STATES
Meagher, Madeleine Joy, Seattle, WA, UNITED STATES
PA Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PI US 2002150922 A1 20021017
AI US 2001-998598 A1 20011116 (9)
PRAI US 2001-304037P 20010710 (60)
US 2001-279670P 20010328 (60)
US 2001-267011P 20010206 (60)
US 2000-252222P 20001120 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 9233
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Stolk, John A., Bothell, WA, UNITED STATES
Xu, Jiangchun, Bellevue, WA, UNITED STATES
Chenault, Ruth A., Seattle, WA, UNITED STATES
Meagher, Madeleine Joy, Seattle, WA, UNITED STATES

L46 ANSWER 11 OF 306 USPATFULL
TI Compositions and methods for the therapy and diagnosis of ovarian cancer
AB Compositions and methods for the therapy and diagnosis of cancer, particularly ovarian cancer, are disclosed. Illustrative compositions comprise one or more ovarian tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly ovarian cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:243051 USPATFULL
TI Compositions and methods for the therapy and diagnosis of ovarian cancer
IN Algate, Paul A., Issaquah, WA, UNITED STATES
Jones, Robert, Seattle, WA, UNITED STATES
Harlocker, Susan L., Seattle, WA, UNITED STATES
PA Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PI US 2002132237 A1 20020919
AI US 2001-867701 A1 20010529 (9)
PRAI US 2000-207484P 20000526 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 25718
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Algate, Paul A., Issaquah, WA, UNITED STATES
Jones, Robert, Seattle, WA, UNITED STATES
Harlocker, Susan L., Seattle, WA, UNITED STATES

L46 ANSWER 12 OF 306 USPATFULL
TI Compositions and methods for the therapy and diagnosis of colon cancer
AB Compositions and methods for the therapy and diagnosis of cancer, particularly colon cancer, are disclosed. Illustrative compositions

comprise one or more colon tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly colon cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:242791 USPATFULL
TI Compositions and methods for the therapy and diagnosis of colon cancer
IN King, Gordon E., Shoreline, WA, UNITED STATES
Meagher, Madeleine Joy, Seattle, WA, UNITED STATES
Xu, Jiangchun, Bellevue, WA, UNITED STATES
Secrist, Heather, Seattle, WA, UNITED STATES
PA Corixa Corporation, Seattle, WA, UNITED STATES (U.S. corporation)
PI US 2002131971 A1 20020919
AI US 2001-33528 A1 20011226 (10)
RLI Continuation-in-part of Ser. No. US 2001-920300, filed on 31 Jul 2001, PENDING
PRAI US 2001-302051P 20010629 (60)
US 2001-279763P 20010328 (60)
US 2000-223283P 20000803 (60)
DT Utility
FS APPLICATION
LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 8083
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN King, Gordon E., Shoreline, WA, UNITED STATES
Meagher, Madeleine Joy, Seattle, WA, UNITED STATES
Xu, Jiangchun, Bellevue, WA, UNITED STATES
Secrist, Heather, Seattle, WA, UNITED STATES

L46 ANSWER 13 OF 306 USPATFULL
TI Selective destruction of cells infected with human immunodeficiency virus
AB Compositions and methods for selectively killing a cell containing a viral **protease** are disclosed. The composition is a variant of a protein synthesis inactivating toxin wherein a viral **protease cleavage** site is interposed between the A and B chains. The variant of the type II ribosome-inactivating protein is activated by digestion of the viral **protease cleavage** site by the specific viral **protease**. The activated ribosome-inactivating protein then kills the cell by inactivating cellular ribosomes. A preferred embodiment of the invention is specific for human immunodeficiency virus (HIV) and uses **ricin** as the ribosome-inactivating protein. In another preferred embodiment of the invention, the variant of the ribosome-inactivating protein is modified by attachment of one or more hydrophobic agents. The hydrophobic agent facilitates entry of the variant of the ribosome-inactivating protein into cells and can lead to incorporation of the ribosome-inactivating protein into viral particles. Still another preferred embodiment of the invention includes a targeting moiety attached to the variants of the ribosome-inactivating protein to target the agent to HIV infectable cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:178548 USPATFULL
TI Selective destruction of cells infected with human immunodeficiency virus
IN Keener, William K., Idaho Falls, ID, UNITED STATES
Ward, Thomas E., Idaho Falls, ID, UNITED STATES

PI US 2002094334 A1 20020718
AI US 2001-785921 A1 20010615 (9)
PRAI US 2000-182759P 20000216 (60)
DT Utility
FS APPLICATION
LREP Stephen R Christian, Bechtel BWXT Idaho, LLC, P O Box 1625, Idaho Falls, ID, 83415-3899
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2066
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Keener, William K., Idaho Falls, ID, UNITED STATES
Ward, Thomas E., Idaho Falls, ID, UNITED STATES

L46 ANSWER 14 OF 306 USPATFULL
TI Feline immunodeficiency virus gene therapy vectors
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency virus, as well as related packaging cell lines, methods for production, and methods of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:133502 USPATFULL
TI Feline immunodeficiency virus gene therapy vectors
IN Johnston, Julie C., Hockessin, DE, UNITED STATES
Sauter, Sybille L., Del Mar, CA, UNITED STATES
Hsu, David Chi-Tang, San Diego, CA, UNITED STATES
Sheridan, Philip Lee, San Diego, CA, UNITED STATES
Hardy, Stephen F., San Francisco, CA, UNITED STATES
Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Yee, Jiing-Kuan, Arcadia, CA, UNITED STATES
PA CHIRON CORPORATION (U.S. corporation)
PI US 2002068354 A1 20020606
AI US 2001-797518 A1 20010301 (9)
RLI Continuation-in-part of Ser. No. US 1999-231235, filed on 15 Jan 1999, PENDING
PRAI US 1998-71731P 19980116 (60)
US 1998-86825P 19980526 (60)
US 1999-114955P 19990104 (60)
DT Utility
FS APPLICATION
LREP CHIRON CORPORATION, Intellectual Property - R 440, P. O. Box 8097, Emeryville, CA, 94662-8097
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 5809
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Johnston, Julie C., Hockessin, DE, UNITED STATES
Sauter, Sybille L., Del Mar, CA, UNITED STATES
Hsu, David Chi-Tang, San Diego, CA, UNITED STATES
Sheridan, Philip Lee, San Diego, CA, UNITED STATES
Hardy, Stephen F., San Francisco, CA, UNITED STATES
Dubensky, Thomas W., JR., Piedmont, CA, UNITED STATES
Yee, Jiing-Kuan, Arcadia, CA, UNITED STATES

L46 ANSWER 15 OF 306 USPATFULL
TI FELINE IMMUNODEFICIENCY VIRUS GENE THERAPY VECTORS
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency virus, as well as related packaging cell lines, methods for production, and methods of use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:92287 USPATFULL
TI FELINE IMMUNODEFICIENCY VIRUS GENE THERAPY VECTORS

IN JOHNSTON, JULIE C., WILMINGTON, DE, UNITED STATES
SAUTER, SYBILLE L., DEL MAR, CA, UNITED STATES
HSU, DAVID CHI-TANG, SAN DIEGO, CA, UNITED STATES
SHERIDAN, PHILIP LEE, SAN DIEGO, CA, UNITED STATES
HARDY, STEPHEN F., SAN FRANCISCO, CA, UNITED STATES
DUBENSKY, THOMAS W., JR., PIEDMONT, CA, UNITED STATES
YEE, JIING-KUAN, DEL MAR, CA, UNITED STATES
PI US 2002048805 A1 20020425
AI US 1999-231235 A1 19990115 (9)
PRAI US 1998-71731P 19980116 (60)
US 1998-86825P 19980526 (60)
DT Utility
FS APPLICATION
LREP Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA, 94662-8097
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 5499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN JOHNSTON, JULIE C., WILMINGTON, DE, UNITED STATES
SAUTER, SYBILLE L., DEL MAR, CA, UNITED STATES
HSU, DAVID CHI-TANG, SAN DIEGO, CA, UNITED STATES
SHERIDAN, PHILIP LEE, SAN DIEGO, CA, UNITED STATES
HARDY, STEPHEN F., SAN FRANCISCO, CA, UNITED STATES
DUBENSKY, THOMAS W., JR., PIEDMONT, CA, UNITED STATES
YEE, JIING-KUAN, DEL MAR, CA, UNITED STATES

L46 ANSWER 16 OF 306 USPATFULL
TI **RECOMBINANT** FUSION PROTEINS BASED ON RIBOSOME-INACTIVATING PROTEINS OF THE MISTLETOE VISCUM ALBUM
AB The invention relates to nucleic acid molecules which encode fusion proteins which contain as components at least one effector module, a processing module and a targeting module. The nucleic acid molecules according to the invention preferably also encode a modulator module and/or an affinity module. The invention furthermore relates to vectors containing these nucleic acid molecules, hosts transformed with the vectors according to the invention, fusion proteins encoded by nucleic acids according to the invention or produced by the hosts according to the invention as well as to medicaments containing the polypeptides or vectors according to the invention. These medicaments are particularly significant for the therapy of diseases associated with a pathological reproduction and/or increased activity of cell populations. A temporary, periodic and strong proliferation, infiltration and immune activity of cells of the immune system is found in autoimmune diseases and allergies, the specificity of these immune cells being due to their reaction to a particular antigen or allergen. These medicaments may also be advantageously used for treating tumors. The polypeptides and vectors described in the present invention may be used to develop medicaments and to test toxin activity-modulating factors. The invention thus also concerns corresponding processes, uses and kits. The modules, with the exception of the affinity and the targeting module, are preferably encoded by nucleic acids extracted or derived from the mistletoe lectin proprotein coding sequence.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:85168 USPATFULL
TI **RECOMBINANT** FUSION PROTEINS BASED ON RIBOSOME-INACTIVATING PROTEINS OF THE MISTLETOE VISCUM ALBUM
IN ECK, JURGEN, HEPPENHEIM, GERMANY, FEDERAL REPUBLIC OF
SCHMIDT, ARNO, BUTTELBORN, GERMANY, FEDERAL REPUBLIC OF
ZINKE, HOLGER, BICKENBACH, GERMANY, FEDERAL REPUBLIC OF
PI US 2002045208 A1 20020418
AI US 1999-347064 A1 19990702 (9)
RLI Continuation of Ser. No. WO 1998-EP9, filed on 2 Jan 1998, UNKNOWN

DT Utility
FS APPLICATION
LREP AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P., ONE COMMERCE SQUARE, 2005 MARKET STREET, SUITE 2200, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 36 Drawing Page(s)
LN.CNT 3070
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN ECK, JURGEN, HEPPENHEIM, GERMANY, FEDERAL REPUBLIC OF
SCHMIDT, ARNO, BUTTELBORN, GERMANY, FEDERAL REPUBLIC OF
ZINKE, HOLGER, BICKENBACH, GERMANY, FEDERAL REPUBLIC OF

L46 ANSWER 17 OF 306 USPATFULL
TI Chimeric gene constructs
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:332612 USPATFULL
TI Chimeric gene constructs
IN Gruber, Harry E., P.O. Box 675272, Rancho Santa Fe, CA, United States 92067
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 3370 Goldfinch St., San Diego, CA, United States 92103
PI US 6495349 B1 20021217
AI US 1995-462512 19950605 (8)
RLI Division of Ser. No. US 1993-136739, filed on 12 Oct 1993, now patented, Pat. No. US 5716826 Continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned Continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Guzo, David
LREP Pochopien, Donald, Dollard, Anne S., Blackburn, Robert P.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 3215
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., P.O. Box 675272, Rancho Santa Fe, CA, United States 92067
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 3370 Goldfinch St., San Diego, CA, United States 92103

L46 ANSWER 18 OF 306 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
AB Isolated nucleic acid molecules are disclosed, comprising an alphavirus nonstructural protein gene which, when operably incorporated into a

recombinant alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:268880 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
IN Dubensky, Jr., Thomas W., Del Mod, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilya, St. Louis, MO, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6465634 B1 20021015
AI US 1999-415900 19991008 (9)
RLI Division of Ser. No. US 1997-944645, filed on 6 Oct 1997 Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, now abandoned Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Wortman, Donna C.
LREP Dollard, Anne S., Blackburn, Robert P., Pasternak, Dahna
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 8244
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Del Mod, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilya, St. Louis, MO, United States

L46 ANSWER 19 OF 306 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
AB Isolated nucleic acid molecules are disclosed, comprising an alphavirus nonstructural protein gene which, when operably incorporated into a **recombinant** alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:254196 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
IN Dubensky, Jr., Thomas W., Del Mar, CA, United States
Polo, John M., Encinitas, CA, United States

Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilva, St. Louis, MO, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6458560 B1 20021001
AI US 1999-415868 19991008 (9)
RLI Division of Ser. No. US 1997-944645, filed on 6 Oct 1997
Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, now abandoned Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Wortman, Donna C.
LREP Dollard, Anne S., Cullman, Louis C., Blackburn, Robert P.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 8154
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Del Mar, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilva, St. Louis, MO, United States

L46 ANSWER 20 OF 306 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
AB Isolated nucleic acid molecules are disclosed, comprising an alphavirus nonstructural protein gene which, when operably incorporated into a **recombinant** alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:238871 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
IN Dubensky, Jr., Thomas W., Del Mar, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilya, St. Louis, MO, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6451592 B1 20020917
AI US 1997-944465 19971006 (8)
RLI Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, now abandoned Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, now abandoned
DT Utility
FS GRANTED

EXNAM Primary Examiner: Wortman, Donna C.
LREP Dollard, Anne S., Cullman, Louis C., Blackburn, Robert P.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 8461
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Del Mar, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilya, St. Louis, MO, United States

L46 ANSWER 21 OF 306 USPATFULL
TI Alphavirus structural protein expression cassettes
AB Isolated nucleic acid molecules are disclosed. comprising an alphavirus nonstructural protein gene which, when operably incorporated into a **recombinant** alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:188229 USPATFULL
TI Alphavirus structural protein expression cassettes
IN Dubensky, Jr., Thomas W., Piedmont, CA, United States
Polo, John M., Encinitas, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Frolov, Ilya, St. Louis, MO, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Washingto University, St. Louis, MO, United States (U.S. corporation)
PI US 6426196 B1 20020730
AI US 1999-415785 19991008 (9)
RLI Division of Ser. No. US 1997-944465, filed on 6 Oct 1997 Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, now abandoned Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Wortman, Donna C.
LREP Blackburn, Robert P., Pasternak, Dahna, Dollard, Anne S.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 8254
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Piedmont, CA, United States
Polo, John M., Encinitas, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Frolov, Ilya, St. Louis, MO, United States

L46 ANSWER 22 OF 306 USPATFULL
TI Compositions and methods for producing **recombinant** virions
AB The invention provides host cells comprising a translation operator sequence (TOP) and packaging elements. Also provided are viral vectors comprising a TOP operably linked to a transgene. Also provided are methods of using these host cells and viral vectors to produce **recombinant** virions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:181564 USPATFULL
TI Compositions and methods for producing **recombinant** virions
IN Hardy, Stephen F., San Francisco, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6423544 B1 20020723
AI US 2000-608730 20000630 (9)
RLI Continuation-in-part of Ser. No. US 1999-476299, filed on 30 Dec 1999, now patented, Pat. No. US 6242259
PRAI US 1998-114732P 19981231 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Schwartzman, Robert A.; Assistant Examiner: Davis, Katharine F
LREP Blackburn, Robert P., Dollard, Anne S., Pasternak, Dahna S.
CLMN Number of Claims: 33
ECL Exemplary Claim: 10
DRWN 22 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2226
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Hardy, Stephen F., San Francisco, CA, United States

L46 ANSWER 23 OF 306 USPATFULL
TI Method for inhibiting human tumor cells
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:152470 USPATFULL
TI Method for inhibiting human tumor cells
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
Barber, Jack R., San Diego, CA, United States
St. Louis, Daniel C., Rockville, MD, United States
Chada, Sunil D., Vista, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Warner, John F., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6410326 B1 20020625
AI US 1995-486683 19950607 (8)
RLI Division of Ser. No. US 1994-344743, filed on 23 Nov 1994 Continuation of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned Continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned Continuation of Ser. No. US 1990-586603, filed on 21 Sep 1990, now abandoned Continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned Continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned Continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Yucel, Remy

LREP Blackburn, Robert P., Pochopien, Donald, Dollard, Anne S.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 54 Drawing Figure(s); 44 Drawing Page(s)
LN.CNT 4484
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
Barber, Jack R., San Diego, CA, United States
St. Louis, Daniel C., Rockville, MD, United States
Chada, Sunil D., Vista, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Warner, John F., San Diego, CA, United States

L46 ANSWER 24 OF 306 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
AB Isolated nucleic acid molecules are disclosed, comprising an alphavirus nonstructural protein gene which, when operably incorporated into a **recombinant** alphavirus particle, eukaryotic layered vector initiation system, or RNA vector replicon, has a reduced level of vector-specific RNA synthesis, as compared to wild-type, and the same or greater level of proteins encoded by RNA transcribed from the viral junction region promoter, as is compared to a wild-type **recombinant** alphavirus particle. Also disclosed are RNA vector replicons, alphavirus vector constructs, and eukaryotic layered vector initiation systems which contain the above-identified nucleic acid molecules.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:116068 USPATFULL
TI **Recombinant** alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis
IN Dubensky, Jr., Thomas W., Del Mon, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States
Frolov, Ilya, St. Louis, MO, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6391632 B1 20020521
AI US 1999-415784 19991008 (9)
RLI Division of Ser. No. US 1997-944465, filed on 6 Oct 1997 Continuation-in-part of Ser. No. US 1997-833148, filed on 4 Apr 1997, now abandoned Continuation-in-part of Ser. No. US 1996-679640, filed on 12 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-668953, filed on 24 Jun 1996, now abandoned Continuation-in-part of Ser. No. US 1996-628594, filed on 5 Apr 1996, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Wortman, Donna C.
LREP Dollard, Anne S., Cullman, Louis C., Blackburn, Robert P.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 8166
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Del Mon, CA, United States
Polo, John M., Encinitas, CA, United States
Belli, Barbara A., San Diego, CA, United States
Schlesinger, Sondra, St. Louis, MO, United States
Dryga, Sergey A., Fort Collins, CO, United States

Frolov, Ilya, St. Louis, MO, United States

L46 ANSWER 25 OF 306 USPATFULL
TI **Recombinant** alphavirus particles
AB Disclosed are **recombinant** alphavirus particles comprising a) an alphavirus vector construct which directs the expression of a heterologous nucleic acid molecule; b) a capsid protein; and c) an envelope glycoprotein from a virus different from said alphavirus vector.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:88256 USPATFULL
TI **Recombinant** alphavirus particles
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Driver, David A., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6376236 B1 20020423
AI US 1999-236140 19990122 (9)
RLI Division of Ser. No. US 1995-404796, filed on 15 Mar 1995, now patented, Pat. No. US 6015686 Continuation-in-part of Ser. No. US 1995-376184, filed on 18 Jan 1995, now abandoned Continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned Continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned Continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Brusca, John S.
LREP McMasters, David D., Dollard, Anne S., Blackburn, Robert P.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 9308
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Driver, David A., San Diego, CA, United States

L46 ANSWER 26 OF 306 USPATFULL
TI Eukaryotic layered vector initiation systems for production of **recombinant** proteins
AB The present invention provides compositions and methods for utilizing **recombinant** alphavirus vectors. Also disclosed are compositions and methods for making and utilizing eukaryotic layered vector initiation systems.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2002:19196 USPATFULL
TI Eukaryotic layered vector initiation systems for production of **recombinant** proteins
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Driver, David A., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6342372 B1 20020129
AI US 1999-350399 19990708 (9)
RLI Continuation of Ser. No. US 1997-931783, filed on 16 Sep 1997, now abandoned Division of Ser. No. US 1995-404796, filed on 15 Mar 1995, now patented, Pat. No. US 6015686 Continuation-in-part of Ser. No. US 1995-376184, filed on 20 Jan 1995, now abandoned Continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned Continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994,

now abandoned Continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Brusca, John S.
LREP McMasters, David D., Dollard, Anne S., Blackburn, Robert P.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10217
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Driver, David A., San Diego, CA, United States

L46 ANSWER 27 OF 306 USPATFULL DUPLICATE 3
TI Antiviral ricin-like proteins
AB The present invention provides a protein having an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker amino acid sequence, linking the A and B chains. The linker sequence contains a **cleavage** recognition site for a retroviral **protease**. The invention also relates to a nucleic acid molecule encoding the protein and to expression vectors incorporating the nucleic acid molecule. Also provided is a method of inhibiting or destroying mammalian cells infected with a retrovirus utilizing the proteins of the invention and pharmaceutical compositions for treating HIV infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:235228 USPATFULL
TI Antiviral ricin-like proteins
IN Borgford, Thor, Burnaby, Canada
PA Twinstrand Therapeutics Inc., Vancouver, Canada (non-U.S. corporation)
PI US 6333303 B1 20011225
WO 9741233 19971106
AI US 1999-147208 19990302 (9)
WO 1997-CA288 19970429
19990302 PCT 371 date
19990302 PCT 102(e) date
PRAI US 1996-16509P 19960430 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Stucker, Jeffrey
LREP Gravelle, MichelineBereskin & Parr
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 2013
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Borgford, Thor, Burnaby, Canada

L46 ANSWER 28 OF 306 USPATFULL
TI Method for treating brain cancer with a conditionally lethal gene
AB The present invention provides **recombinant** viral vectors carrying a vector construct which directs the expression of a gene product (e.g., HSVTK) that activates a compound with little or no cytotoxicity into a toxic product. Also provided are methods of destroying or inhibiting pathogenic agents in a warm blooded animal, comprising the step of administering to the animal a viral vector such as that described above, in order to inhibit or destroy the pathogenic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:82308 USPATFULL
TI Method for treating brain cancer with a conditionally lethal gene

IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6241982 B1 20010605
AI US 1995-468646 19950606 (8)
RLI Division of Ser. No. US 1993-155944, filed on 18 Nov 1993, now abandoned Continuation-in-part of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned Continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned Continuation of Ser. No. US 1990-586603, filed on 21 Sep 1990, now abandoned Continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned Continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned Continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartzman, Robert A.
LREP Pochopien, Donald, Dollard, Anne, Blackburn, Robert
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN 30 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 2796
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States

L46 ANSWER 29 OF 306 USPATFULL
TI Anti-pathogen system and methods of use thereof
AB The present invention provides an anti-pathogen system comprising one or more fusion proteins that includes a transduction domain and a cytotoxic domain. The cytotoxic domain is specifically activated by a pathogen infection. The anti-pathogen system effectively kills or injures cells infected by one or a combination of different pathogens. Further provided are protein transduction domains that provide enhanced transduction efficiency.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:59379 USPATFULL
TI Anti-pathogen system and methods of use thereof
IN Dowdy, Steven F., Clayton, MO, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 6221355 B1 20010424
AI US 1998-208966 19981210 (9)
PRAI US 1998-82402P 19980420 (60)
US 1997-69012P 19971210 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Park, Hankyel T.
LREP Buchanan, Robert L., Schray, Kerri Pollard, Corless, Peter F.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 26 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 3168
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dowdy, Steven F., Clayton, MO, United States

L46 ANSWER 30 OF 306 WPIDS (C) 2003 THOMSON DERWENT
TI New polynucleotide, useful for treating prostatic cancer, comprises prostate specific chimeric enhancer and proximal promoter sequence operably linked to nucleic acid encoding heterologous polypeptide.
AN 2001-273768 [28] WPIDS
AB WO 200127256 A UPAB: 20010522
NOVELTY - An isolated polynucleotide (I) comprising a prostate-specific chimeric enhancer (PSE) sequence and a proximal promoter sequence operably

linked to a nucleic acid segment that encodes a heterologous polypeptide, where PSE contains an androgen response element (ARE) and specifically activates transcription of the nucleic acid segment in a mammalian prostate cell, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a genetic construct (II) comprising a wildtype PSE, an artificial PSE and a prostate-specific promoter sequence operably linked to a nucleic acid segment that encodes a heterologous polypeptide, where the wildtype PSE contains a prostate specific antigen (PSA) enhancer sequence and the artificial PSE contains AGAACAGCAAGTGCT (S1), AGAACAGCAAGTACT (S2), GGAACATATTGTATT (S3) or GGAACATATTGTATC (S4), which specifically activate transcription of the nucleic acid segment in a mammalian prostate cell;

(2) a plasmid vector (III) comprising (I) or (II);

(3) a viral vector (IV) for transfection of mammalian cells comprising (I) or (II);

(4) a host cell (V) comprising (I), (II), (III) or (IV);

(5) a kit comprising (I), (II), (III) or (IV) and instructions for use; and

(6) expressing a heterologous polypeptide in a human prostate cell comprising expressing in the cell (I), (II), (III) or (IV) and growing the cell under expression conditions.

ACTIVITY - Cytostatic. Experimental protocols are described but no supporting data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I), (II), (III) and (IV) are useful (in the manufacture of a medicament) for the treatment of a prostate disorder or a metasized prostate cancer, such as hyperplasia and hyperproliferation of prostate cells, in a human. They are also useful for directing the tissue-specific expression of a heterologous polypeptide in a human prostate cell comprising administering (I)-(IV) by injection, infection, transformation, liposome-mediated transfection, polybrene-mediated transfection, receptor-mediated uptake or Ca-PO4-mediated transformation (claimed).

ADVANTAGE - The ARE4 enhancer comprises 4 tandem copies of the ARE element which displays more than 100 fold androgen inducible activity in transfection assays. The therapeutic compounds also avoid many of the unwanted side effects of conventional therapies, avoid invasive surgical procedures and are effective in lower and less frequent administration.

Dwg.0/18

AN 2001-273768 [28] WPIDS
DNC C2001-083073
TI New polynucleotide, useful for treating prostatic cancer, comprises prostate specific chimeric enhancer and proximal promoter sequence operably linked to nucleic acid encoding heterologous polypeptide.
DC B04 D16
IN BELLDEGRUN, A S; CAREY, M F; WU, L
PA (REGC) UNIV CALIFORNIA SYSTEM
CYC 94
PI WO 2001027256 A2 20010419 (200128)* EN 111p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001012038 A 20010423 (200147)
ADT WO 2001027256 A2 WO 2000-US28444 20001013; AU 2001012038 A AU 2001-12038 20001013
FDT AU 2001012038 A Based on WO 200127256
PRAI US 1999-159730P 19991015; US 1999-159691P 19991014
IN BELLDEGRUN, A S; CAREY, M F; WU, L

L46 ANSWER 31 OF 306 WPIDS (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer.

AN 2001-300164 [31] WPIDS

AB WO 200125267 A UPAB: 20010607

NOVELTY - A **recombinant** protein (I) comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker (L) amino acid sequence that links the A and B chains and comprising a **cleavage** recognition site for a specific **protease**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a purified and isolated nucleic acid molecule (II) comprising:

(a) a nucleotide sequence encoding an A chain of a ricin-like toxin;

(b) a nucleotide sequence encoding a B chain of a ricin-like toxin; and

(c) a nucleotide sequence encoding (L);

(2) a plasmid incorporating (II);

(3) a baculovirus transfer vector incorporating (II);

(4) preparing a pharmaceutical for treating a cell having a specific protease, by preparing and introducing (II) into a host cell, expressing (II) in the host cell to obtain (I), and suspending the protein in a pharmaceutically acceptable carrier, diluent or excipient;

(5) a pharmaceutical composition (PC) for treating cancer and inflammation comprising (I);

(6) a pharmaceutical composition for treating a cell having a specific protease, comprising (I) or (II);

(7) a purified and isolated nucleic acid molecule comprising a nucleic acid sequence of pAP301, pAP302, pAP303, pAP304, pAP305, pAP308, pAP309, pAP313, pAP314, pAP315, pAP316, pAP318, pAP320, pAP321, pAP322, pAP323, pAP324 or pAP325, sequences being fully defined in the specification;

(8) inhibiting or destroying cells having a specific protease comprising:

(a) preparing (II);

(b) introducing (II) into a host cell and expressing (II) to obtain (I);

(c) suspending (I) in a pharmaceutically acceptable carrier, diluent or excipient; and

(d) contacting the cells with the **recombinant** protein; and

(9) a linker protein comprising an amino acid sequence of PAP301, PAP302, PAP303, PAP304, PAP305, PAP308, PAP309, PAP313, PAP314, PAP315, PAP316, PAP318, PAP320, PAP321, PAP322, PAP323, PAP324 or PAP325, the sequences being fully defined in the specification.

ACTIVITY - Cytostatic; antiinflammatory; antirheumatic; antiarthritic; antiarteriosclerotic; neuroprotective.

BDF-1 mice, grouped according to body weight, were inoculated with 1 multiply 106 cells implanted subcutaneously in the flank. P388 murine leukemia cells from the ATCC tumor repository were maintained as an ascitic fluid in the BDF-1 mouse which were passaged to new mice weekly. The cells used for experiment were used within passage 3-20. The cells were rinsed with Hanks Balanced Salt Solution, counted on a hemocytometer and diluted with HBSS to a concentration of 20 multiply 106 cells/ml. PAP034 was injected intravenously on days 3,6 and 9 after tumor injection. The results showed a significant delay in tumor growth in the murine tumor model.

MECHANISM OF ACTION - None given.

USE - (II) is useful for inhibiting or destroying cells having a specific protease e.g., cancer cell found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease, by introducing (II) into a host cell and expressing (II) in the host cell to obtain (I), and contacting the diseased cells with (I). (I) is also useful for inhibiting or destroying cells having a

specific protease. PC is useful for treating cancer and inflammation (claimed).

ADVANTAGE - (I) has the specificity for cells that contain a specific protease, including those of inflammatory disorders and cancer cells, without the need for a cell binding component.

Dwg.0/22

AN 2001-300164 [31] WPIDS
DNC C2001-092131
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer.
DC B04 D16
IN BORGFORD, T; BRAUN, C; PURAC, A
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC
CYC 94
PI WO 2001025267 A2 20010412 (200131)* EN 146p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000076368 A 20010510 (200143)
ADT WO 2001025267 A2 WO 2000-CA1162 20001004; AU 2000076368 A AU 2000-76368 20001004
FDT AU 2000076368 A Based on WO 200125267
PRAI US 2000-197409P 20000414; US 1999-157807P 19991004
IN BORGFORD, T; BRAUN, C; PURAC, A

L46 ANSWER 32 OF 306 USPATFULL
TI Replication defective viral vectors for infecting human cells
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:138119 USPATFULL
TI Replication defective viral vectors for infecting human cells
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6133029 20001017
AI US 1995-479672 19950606 (8)
RLI Continuation of Ser. No. US 1994-344743, filed on 23 Nov 1994, now abandoned which is a continuation of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned which is a continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned which is a continuation of Ser. No. US 1990-586603, filed on 21 Sep 1990, now abandoned which is a continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988,

now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartzman, Robert A.
LREP Pochopien, Donald J., Blackburn, Robert P.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 48 Drawing Figure(s); 44 Drawing Page(s)
LN.CNT 4508
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States

L46 ANSWER 33 OF 306 USPATFULL
TI Hybrid molecules having translocation region and cell-binding region
AB Disclosed is a hybrid molecule comprising a first part, a second part, and a third part connected by covalent bonds,

(a) wherein said first part comprises a portion of the binding domain of a cell-binding polypeptide ligand effective to cause said hybrid protein to bind to a cell of an animal;

(b) wherein said second part comprises a portion of a translocation domain of naturally occurring protein which translocates said third part across the cytoplasmic membrane into the cytosol of the cell; and

(c) wherein said third part comprises a chemical entity to be introduced into the cell, wherein each of said first part and said third part is non-native with respect to said naturally occurring protein, and further wherein said covalent bond connecting said second part and said third part is a cleavable bond, provided that when said second part comprises a portion of a translocation domain of Pseudomonas exotoxin, said third part is not a polypeptide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:15726 USPATFULL
TI Hybrid molecules having translocation region and cell-binding region
IN Murphy, John R., Boston, MA, United States
PA Seragen, Inc., Hopkinton, MA, United States (U.S. corporation)
PI US 6022950 20000208
AI US 1995-479510 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1993-102387, filed on 4 Aug 1993, now patented, Pat. No. US 5668255 which is a continuation of Ser. No. US 1991-722484, filed on 27 Jun 1991, now abandoned which is a continuation-in-part of Ser. No. US 1990-538276, filed on 14 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-456095, filed on 22 Dec 1989, now abandoned which is a continuation-in-part of Ser. No. US 1985-742554, filed on 7 Jun 1985, now abandoned which is a continuation-in-part of Ser. No. US 1985-726808, filed on 25 Apr 1985, now abandoned which is a continuation of Ser. No. US 1984-618199, filed on 7 Jun 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Schwartzman, Robert
LREP Lerner, David, Littenberg, Krumholz & Mentlik, LLP
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 1127
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Murphy, John R., Boston, MA, United States

L46 ANSWER 34 OF 306 USPATFULL

TI Method for stimulating an immune response utilizing **recombinant** alphavirus particles
AB The present invention provides compositions and methods for utilizing **recombinant** alphavirus vectors. Also disclosed are compositions and methods for making and utilizing eukaryotic layered vector initiation systems.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:7195 USPATFULL
TI Method for stimulating an immune response utilizing **recombinant** alphavirus particles
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Chang, Steven M.W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 6015694 20000118
AI US 1997-931869 19970916 (8)
RLI Division of Ser. No. US 1995-404796, filed on 15 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-376184, filed on 18 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Brusca, John S.
LREP McMasters, David D., Blackburn, Robert P.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10431
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Chang, Steven M.W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States

L46 ANSWER 35 OF 306 USPATFULL
TI Eukaryotic layered vector initiation systems
AB The present invention provides compositions and methods for utilizing **recombinant** alphavirus vectors. Also disclosed are compositions and methods for making and utilizing eukaryotic layered vector initiation systems.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000:7187 USPATFULL
TI Eukaryotic layered vector initiation systems
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States
PA Chiron Viagene, Inc., Emeryville, CA, United States (U.S. corporation)
PI US 6015686 20000118
AI US 1995-404796 19950315 (8)
RLI Continuation-in-part of Ser. No. US 1995-376184, filed on 20 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Brusca, John S.

LREP Seed & Berry, Kruse, Norman J., Blackburn, Robert P.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10466
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States

L46 ANSWER 36 OF 306 USPATFULL
TI Method for treating a metastatic carcinoma using a conditionally lethal gene
AB The present invention provides **recombinant** viral vectors carrying a vector construct which directs the expression of a gene product (e.g., HSVTK) that activates a compound with little or no cytotoxicity into a toxic product. Also provided are methods of destroying or inhibiting pathogenic agents in a warm blooded animal, comprising the step of administering to the animal a viral vector such as that described above, in order to inhibit or destroy the pathogenic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1999:159476 USPATFULL
TI Method for treating a metastatic carcinoma using a conditionally lethal gene
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5997859 19991207
AI US 1995-467034 19950606 (8)
RLI Division of Ser. No. US 1993-155944, filed on 18 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned which is a continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned which is a continuation of Ser. No. US 1990-586603, filed on 21 Sep 1990, now abandoned which is a continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Pochopien, Donald J., Blackburn, Robert P.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 30 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 2772
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Barber, Jack R., San Diego, CA, United States
Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States

L46 ANSWER 37 OF 306 USPATFULL
TI **Recombinant** DNAS encoding three-part hybrid proteins
AB Disclosed is a **recombinant** DNA molecule encoding a hybrid protein comprising a first part, a second part, and a third part,

(a) wherein said first part comprises a portion of the binding domain of a cell-binding polypeptide ligand effective to cause said hybrid protein to bind to a cell of an animal;

(b) wherein said second part comprises a portion of a translocation domain of naturally occurring protein selected from the group consisting of diphtheria toxin, botulinum neurotoxin, ricin, cholera toxin, LT toxin, C3 toxin, Shiga toxin, Shiga-like toxin, pertussis toxin and tetanus toxin, which translocates said third part across the cytoplasmic membrane into the cytosol of the cell; and

(c) wherein said third part comprises a polypeptide entity to be introduced into the cell, wherein said third part is non-native with respect to said naturally occurring protein of (b).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1999:124742 USPATFULL
TI **Recombinant** DNAS encoding three-part hybrid proteins
IN Murphy, John R., Wayland, MA, United States
PA Seragen, Inc., Hopkinton, MA, United States (U.S. corporation)
PI US 5965406 19991012
AI US 1995-488246 19950607 (8)
RLI Division of Ser. No. US 1993-102387, filed on 4 Aug 1993, now patented, Pat. No. US 5668255 which is a continuation of Ser. No. US 1991-722484, filed on 27 Jun 1991, now abandoned which is a continuation-in-part of Ser. No. US 1990-538276, filed on 14 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-456095, filed on 22 Dec 1989, now abandoned which is a continuation-in-part of Ser. No. US 1985-742554, filed on 7 Jun 1985, now abandoned which is a continuation-in-part of Ser. No. US 1985-726808, filed on 25 Apr 1985, now abandoned which is a continuation of Ser. No. US 1984-618199, filed on 7 Jun 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Schwartzman, Robert
LREP Lerner, David, Littenberg, Krumholz & Mentlik, LLP
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 1160
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Murphy, John R., Wayland, MA, United States

L46 ANSWER 38 OF 306 USPATFULL
TI **Recombinant** retroviruses
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1999:39929 USPATFULL
TI **Recombinant** retroviruses
IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050 H Via Alicante Dr., La Jolla, CA, United States 92037
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130

PI US 5888502 19990330
AI US 1995-463122 19950605 (8)
RLI Division of Ser. No. US 1993-136739, filed on 12 Oct 1993, now patented, Pat. No. US 5716826 which is a continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Kruse, Norman J., Pochopien, Donald J., Blackburn, Robert P.
CLMN Number of Claims: 72
ECL Exemplary Claim: 19
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 3337
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050 H Via Alicante Dr., La Jolla, CA, United States 92037
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130

L46 ANSWER 39 OF 306 USPATFULL
TI Method for making reflection defective retroviral vectors for infecting human cells
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1999:1521 USPATFULL
TI Method for making reflection defective retroviral vectors for infecting human cells
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
Barber, Jack R., San Diego, CA, United States
St. Louis, Daniel C., Rockville, MD, United States
Chada, Sunil D., Vista, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Warner, John F., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5856185 19990105
AI US 1995-472109 19950607 (8)
RLI Continuation of Ser. No. US 1994-344743, filed on 23 Nov 1994, now abandoned which is a continuation of Ser. No. US 1993-139994, filed on 20 Oct 1993, now abandoned which is a continuation of Ser. No. US 1992-965084, filed on 22 Oct 1992, now abandoned which is a continuation of Ser. No. US 1990-586603, filed on 21 Sep 1990, now abandoned which is a continuation-in-part of Ser. No. US 1990-565606, filed on 10 Aug 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988,

now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Pochopien, Donald, Kruse, Norman J., Blackburn, Robert P.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 54 Drawing Figure(s); 44 Drawing Page(s)
LN.CNT 4588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
Barber, Jack R., San Diego, CA, United States
St. Louis, Daniel C., Rockville, MD, United States
Chada, Sunil D., Vista, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Warner, John F., San Diego, CA, United States

L46 ANSWER 40 OF 306 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 4
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells.
AN 1999-009431 [01] WPIDS
AB WO 9849311 A UPAB: 19990113
New purified and isolated nucleic acid (I) encodes: (i) the A and B chains of a **ricin**-like toxin (II), and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also new are: (1) plasmids or baculovirus transfer vectors that contain (I), and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker.

USE - (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also (not claimed) cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo.

ADVANTAGE - (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus-infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells.

Dwg.45A/67
AN 1999-009431 [01] WPIDS
DNC C1999-003230
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells.
DC B04 C06 D16
IN BORGFORD, T
PA (DNOV-N) DE NOVO ENZYME CORP
CYC 83
PI WO 9849311 A2 19981105 (199901)* EN 351p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG

US UZ VN YU ZW
AU 9870237 A 19981124 (199914)
EP 977862 A2 20000209 (200012) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001523961 W 20011127 (200204) 330p
ADT WO 9849311 A2 WO 1998-CA394 19980430; AU 9870237 A AU 1998-70237 19980430; EP 977862 A2 EP 1998-916743 19980430, WO 1998-CA394 19980430; JP 2001523961 W JP 1998-546437 19980430, WO 1998-CA394 19980430
FDT AU 9870237 A Based on WO 9849311; EP 977862 A2 Based on WO 9849311; JP 2001523961 W Based on WO 9849311
PRAI US 1997-63715P 19971029; US 1997-45148P 19970430
IN BORGFORD, T

L46 ANSWER 41 OF 306 USPATFULL
TI **Recombinant** retroviruses
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:159468 USPATFULL
TI **Recombinant** retroviruses
IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050H Via Alicante Dr., La Jolla, CA, United States 92037
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130
PI US 5851529 19981222
AI US 1995-477890 19950607 (8)
RLI Continuation of Ser. No. US 1993-136739, filed on 12 Oct 1993 which is a continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Kruse, Norman J.Seed & Berry, Blackburn, Robert P.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 3017
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050H Via Alicante Dr., La Jolla, CA, United States 92037
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130

L46 ANSWER 42 OF 306 USPATFULL
TI Alphavirus vector constructs
AB The present invention provides compositions and method,, for utilizing **recombinant** alphavirus vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:150739 USPATFULL
TI Alphavirus vector constructs
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States
Belli, Barbara A., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5843723 19981201
AI US 1996-739167 19961030 (8)
RLI Continuation of Ser. No. US 1995-404796, filed on 20 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-376184, filed on 20 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Brusca, John S.
LREP McMasters, David D., Kruse, Norman J., Blackburn, Robert P.
CLMN Number of Claims: 47
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10318
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States
Belli, Barbara A., San Diego, CA, United States

L46 ANSWER 43 OF 306 USPATFULL
TI Method for destroying a diseased human cell
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:134622 USPATFULL
TI Method for destroying a diseased human cell
IN Gruber, Harry E., P.O. Box 675272, Rancho Santa Fe, CA, United States 92067
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 3370 Goldfinch St., San Diego, CA, United States 92103
PI US 5830458 19981103
AI US 1995-487776 19950607 (8)

RLI Continuation of Ser. No. US 1993-136739, filed on 12 Oct 1993, now patented, Pat. No. US 5716826 which is a continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George D.; Assistant Examiner: Schwartzman, Robert
LREP Kruse, Norman J., Pochopien, Donald J., Blackburn, Robert P.
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 3199
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., P.O. Box 675272, Rancho Santa Fe, CA, United States 92067
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 3370 Goldfinch St., San Diego, CA, United States 92103

L46 ANSWER 44 OF 306 USPATFULL
TI Eukaryotic layered vector initiation systems
AB The present invention provides compositions and methods for utilizing **recombinant** alphavirus vectors. Also disclosed are compositions and methods for making and utilizing eukaryotic layered vector initiation systems.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:119004 USPATFULL
TI Eukaryotic layered vector initiation systems
IN Dubensky, Jr., Thomas W., P.O. Box 675205, Rancho Sante Fe, CA, United States 92067
Polo, John M., 1222 Reed Ave., Number 4, San Diego, CA, United States 92109
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Driver, David A., 5142 Biltmore St., San Diego, CA, United States 92117
PI US 5814482 19980929
AI US 1996-739158 19961030 (8)
RLI Division of Ser. No. US 1995-404796, filed on 15 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-376184, filed on 18 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Brusca, John S.
LREP Seed & Berry, Kruse, Norman J., Blackburn, Robert P.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10431
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., P.O. Box 675205, Rancho Sante Fe, CA, United States 92067
Polo, John M., 1222 Reed Ave., Number 4, San Diego, CA, United States 92109
Jolly, Douglas J., 277 Hillcrest Dr., Leucadia, CA, United States 92024
Driver, David A., 5142 Biltmore St., San Diego, CA, United States 92117

L46 ANSWER 45 OF 306 USPATFULL
TI Alphavirus structural protein expression cassettes

AB The present invention provides compositions and methods for utilizing **recombinant** alphavirus vectors. Also disclosed are compositions and methods for making and utilizing eukaryotic layered vector initiation systems.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:91872 USPATFULL
TI Alphavirus structural protein expression cassettes
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5789245 19980804
AI US 1996-741881 19961030 (8)
RLI Division of Ser. No. US 1995-404796, filed on 15 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-376184, filed on 20 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-348472, filed on 30 Nov 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-198450, filed on 18 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-122791, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James; Assistant Examiner: Brusca, John S.
LREP McMasters, David D., Kruse, Norman J., Blackburn, Robert P.
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 30 Drawing Page(s)
LN.CNT 10270
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Dubensky, Jr., Thomas W., Rancho Sante Fe, CA, United States
Polo, John M., San Diego, CA, United States
Ibanez, Carlos E., San Diego, CA, United States
Chang, Stephen M. W., San Diego, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Driver, David A., San Diego, CA, United States

L46 ANSWER 46 OF 306 USPATFULL
TI Aptamers specific for biomolecules and methods of making
AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:57716 USPATFULL
TI Aptamers specific for biomolecules and methods of making
IN Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States

Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States
PA Gilead Sciences, Inc., Foster City, CA, United States (U.S. corporation)
PI US 5756291 19980526
AI US 1995-484192 19950607 (8)
RLI Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Zitomer, Stephanie W.
LREP Bosse, Mark L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 8242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States
Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States

L46 ANSWER 47 OF 306 USPATFULL
TI **Recombinant** retroviruses
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:14678 USPATFULL
TI **Recombinant** retroviruses
IN Gruber, Harry E., Rancho Santa Fe, CA, United States
Jolly, Douglas J., Leucadia, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
PA Chiron Viagene, Inc., United States (U.S. corporation)
PI US 5716826 19980210
AI US 1993-136739 19931012 (8)
RLI Continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George G.; Assistant Examiner: Schwartzman, Robert
LREP Kruse, Norman J.Seed & Berry, Blackburn, Robert P.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 2895
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Gruber, Harry E., Rancho Santa Fe, CA, United States

Jolly, Douglas J., Leucadia, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States

L46 ANSWER 48 OF 306 USPATFULL
TI **Recombinant** retroviruses
AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 1998:14473 USPATFULL
TI **Recombinant** retroviruses
IN Guber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States
PA Chiron Viagene, Inc., United States (U.S. corporation)
PI US 5716613 19980210
AI US 1995-474736 19950607 (8)
RLI Division of Ser. No. US 1993-136739, filed on 12 Oct 1993 which is a continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George G.; Assistant Examiner: Schwartzman, Robert
LREP Kruse, Norman J.Seed & Berry, Blackburn, Robert P.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 2889
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Guber, Harry E., San Diego, CA, United States
Jolly, Douglas J., La Jolla, CA, United States
Respess, James G., San Diego, CA, United States
Laikind, Paul K., San Diego, CA, United States

L46 ANSWER 49 OF 306 SCISEARCH COPYRIGHT 2003 THOMSON ISI
SO BIOCHEMISTRY, (1 DEC 1998) Vol. 37, No. 48, pp. 16934-16942.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0006-2960.
TI Role of caspases in immunotoxin-induced apoptosis of cancer cells
AB Immunotoxins composed of antibodies linked to plant or bacterial toxins are being evaluated in the treatment of cancer. It is known that the toxin moieties of immunotoxins, including Pseudomonas exotoxin A (PE), diphtheria toxin, and **ricin**, are capable of inducing apoptosis. Since the efficiency of induction of apoptosis and the apoptosis pathway may have direct effects on the therapeutic usefulness of immunotoxins, we have studied how B3(Fv)-PE38, a genetically engineered immunotoxin in which the Fv fragment of an antibody is fused to a mutated form of PE, induces apoptosis of the MCF-7 breast cancer cell line. We show for the first time that a PE-containing immunotoxin activates ICE/ced-3 **proteases**, now termed caspases, and causes characteristic

cleavage of the ''death substrate'' poly(ADP)-ribose polymerase (PARP) to an 89 kDa fragment with a time course of **cleavage** comparable to that induced by TNF alpha. Also the fluorescent substrate? DEVD-AFC, is **cleaved** 2-4-fold more rapidly by lysates from B3(Fv)-PE38 treated MCF-7 cells than untreated control cells, suggesting that a CPP32-like caspase is involved in B3(Fv)-PE38-mediated apoptosis. B3(Fv)-PE38 -induced PARP **cleavage** is inhibited by several **protease** inhibitors known to inhibit caspases (zVAD-fmk, zDEVD-fmk, zIETD-fmk) as well as by overexpression of Bcl-2 providing additional evidence for caspase involvement. zVAD-fmk, a broad spectrum inhibitor of most mammalian caspases, prevents the early morphological changes and loss of cell membrane integrity produced by B3(Fv)-PE38, but not its ability to inhibit protein synthesis, arrest cell growth, and subsequently kill cells. Despite inhibition of apoptosis, the immunotoxin is still capable of selective cell killing, which indicates that B3(Fv)-PE38 kills cells by two mechanisms: one requires caspase activation, and the other is due to the arrest of protein synthesis caused by inactivation of elongation factor 2. The fact that an immunotoxin can specifically kill tumor cells without the need of inducing apoptosis makes such agents especially valuable for the treatment of cancers that are protected against apoptosis, e.g., by overexpression of Bcl-2.

AN 1998:935411 SCISEARCH
GA The Genuine Article (R) Number: 144WX
TI Role of caspases in immunotoxin-induced apoptosis of cancer cells
AU KepplerHafkemeyer A; Brinkmann U; Pastan I (Reprint)
CS NCI, MOL BIOL LAB, DIV BASIC SCI, NIH, BLDG 37, ROOM 4E16, 37 CONVENT DR MSC 4255, BETHESDA, MD 20892 (Reprint); NCI, MOL BIOL LAB, DIV BASIC SCI, NIH, BETHESDA, MD 20892
CYA USA
SO BIOCHEMISTRY, (1 DEC 1998) Vol. 37, No. 48, pp. 16934-16942.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0006-2960.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AU KepplerHafkemeyer A; Brinkmann U; Pastan I (Reprint)

L46 ANSWER 50 OF 306 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
TI Cleavable fusion proteins of ricin analogs for use as antivirals
AB A method of manufg. **ricin** as an inactive precursor that can be activated by **cleavage** by a **protease** specific to a pathogen, i.e. a viral **proteinase**, is described. Specifically, the precursor is a fusion protein of the A and B chains linked by a peptide contg. a cleavage site for a retroviral proteinase such as those from HIV or an HTLV. The active form of the ricin then efficiently kills mammalian cells expressing the gene upon infection with a retrovirus. Expression vectors for these fusion proteins can be used in the treatment of HIV infections and human T-cell leukemias involving HTLV. Manuf. of these fusion proteins in a baculovirus system is demonstrated. The proteinase-cleaved precursor inhibited translation of brome mosaic virus in rabbit reticulocyte lysates.
AN 1997:740313 CAPLUS
DN 128:30381
TI Cleavable fusion proteins of ricin analogs for use as antivirals
IN Borgford, Thor
PA De Novo Enzyme Corporation, Can.; Borgford, Thor
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741233	A1	19971106	WO 1997-CA288	19970429
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2252799	AA	19971106	CA 1997-2252799	19970429
	AU 9723770	A1	19971119	AU 1997-23770	19970429
	EP 909322	A1	19990421	EP 1997-919216	19970429
	R: DE, ES, FR, GB, IT, NL				
PRAI	US 1996-16509P	P	19960430		
	WO 1997-CA288	W	19970429		

IN Borgford, Thor

L46 ANSWER 51 OF 306 USPATFULL

TI **Recombinant** retroviruses expressing a protein that converts a pro-drug into a cytotoxic agent

AB **Recombinant** retroviruses carrying a vector construct capable of preventing, inhibiting, stabilizing or reversing infectious, cancerous or auto-immune diseases are disclosed. More specifically, the **recombinant** retroviruses of the present invention are useful for (a) stimulating a specific immune response to an antigen or a pathogenic antigen; (b) inhibiting a function of a pathogenic agent, such as a virus; and (c) inhibiting the interaction of an agent with a host cell receptor. In addition, eucaryotic cells infected with, and pharmaceutical compositions containing such a **recombinant** retrovirus are disclosed. Various methods for producing **recombinant** retroviruses having unique characteristics, and methods for producing transgenic packaging animals or insects are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 97:109741 USPATFULL

TI **Recombinant** retroviruses expressing a protein that converts a pro-drug into a cytotoxic agent

IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050 Via Alicante Dr., La Jolla, CA, United States 92037
Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130

PI US 5691177 19971125

AI US 1995-460996 19950605 (8)

RLI Division of Ser. No. US 1993-136739, filed on 12 Oct 1993 which is a continuation of Ser. No. US 1989-395932, filed on 18 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-170515, filed on 21 Mar 1988, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Elliott, George G.; Assistant Examiner: Railey, II, Johnny F.

LREP Kruse, Norman J., Pochopien, Donald J., Blackburn, Robert P.

CLMN Number of Claims: 24

ECL Exemplary Claim: 1

DRWN 31 Drawing Figure(s); 27 Drawing Page(s)

LN.CNT 3039

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN Guber, Harry E., 13083 Maritime Pl., San Diego, CA, United States 92130
Jolly, Douglas J., 3050 Via Alicante Dr., La Jolla, CA, United States 92037

Respess, James G., 4966 Lamont St., San Diego, CA, United States 92109
Laikind, Paul K., 12433 Caminito Mira Del Mar, San Diego, CA, United States 92130

L46 ANSWER 52 OF 306 USPATFULL
TI Hybrid molecules having translocation region and cell-binding region
AB A hybrid molecule including a first part and a second part connected by a covalent bond,

(a) the first part including a portion of the binding domain of a cell-binding ligand, which portion is able to cause the hybrid molecule of the invention to bind to an animal cell; and

(b) the second part including a portion of a translocation domain of a protein, provided that (i) the hybrid molecule does not include an enzymatically-active portion of the protein, (ii) the first part and the second part are not segments of the same naturally-occurring polypeptide toxin, and (iii) the portion of the translocation domain, when covalently bonded to the enzymatically-active effector region of a toxin selected from diphtheria toxin, Pseudomonas exotoxin A, cholera toxin, ricin toxin, and Shiga-like toxin, is capable of translocating such effector region across the cytoplasmic membrane of the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 97:84079 USPATFULL
TI Hybrid molecules having translocation region and cell-binding region
IN Murphy, John R., Wayland, MA, United States
PA Seragen, Inc., Hopkinton, MA, United States (U.S. corporation)
PI US 5668255 19970916
AI US 1993-102387 19930804 (8)
RLI Continuation of Ser. No. US 1991-722484, filed on 27 Jun 1991, now abandoned which is a continuation-in-part of Ser. No. US 1990-538276, filed on 14 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-456095, filed on 22 Dec 1989, now abandoned which is a continuation-in-part of Ser. No. US 1985-742554, filed on 7 Jun 1985, now abandoned which is a continuation-in-part of Ser. No. US 1985-726808, filed on 25 Apr 1985, now abandoned which is a continuation of Ser. No. US 1984-618199, filed on 7 Jun 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Lerner, David, Littenberg, Krumholz & Mentlik
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 977
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Murphy, John R., Wayland, MA, United States

L46 ANSWER 53 OF 306 USPATFULL
TI Chemotactic, antibiotic and lipopolysaccharide-binding peptide fragments of CAP37
AB Disclosed is a homogeneously pure monocyte chemotactic protein, CAP37, and the entire coding sequences for unprocessed and mature human CAP37 protein. Further, the **recombinant** production, from nucleic acid coding sequences, of mature CAP37 protein and the mature protein with amino-terminal and/or carboxy-terminal extensions is described. Also disclosed are methods to identify and recombinantly produce bioactive peptides derived from the CAP37 protein coding sequence which are effective chemoattractants of monocytes and/or are capable of binding bacterial lipopolysaccharide. A method of preparing homogeneously pure CAP37 using hydrophobic HPLC is described. Bioactive peptide fragments of CAP37 having chemotactic, antibacterial and/or LPS-binding activity are disclosed. Finally, methods of treating wounds,

diseased tissue, such as tumors, and infections are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 96:5884 USPATFULL
TI Chemotactic, antibiotic and lipopolysaccharide-binding peptide fragments of CAP37
IN Pereira, Heloise A., Decatur, GA, United States
Spitznagel, John K., Decatur, GA, United States
PA Emory University, Atlanta, GA, United States (U.S. corporation)
PI US 5484885 19960116
AI US 1992-855417 19920319 (7)
RLI Continuation-in-part of Ser. No. US 1990-543151, filed on 25 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-375739, filed on 5 Jul 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Furman, Keith C.
LREP Needle & Rosenberg
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 2498
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IN Pereira, Heloise A., Decatur, GA, United States
Spitznagel, John K., Decatur, GA, United States

L46 ANSWER 54 OF 306 USPATFULL
TI Method of increasing monocyte chemotaxis with CAP37 and monocyte chemotactic portions thereof
AB Disclosed is a homogeneously pure monocyte chemotactic protein, CAP37, and the entire coding sequences for unprocessed and mature human CAP37 protein. Further, the **recombinant** production, from nucleic acid coding sequences, of mature CAP37 protein and the mature protein with amino-terminal and/or carboxy-terminal extensions is described. Also disclosed are methods to identify and recombinantly produce bioactive peptides derived from the CAP37 protein coding sequence which are effective chemoattractants monocytes and/or are capable of binding bacterial lipopolysaccharide. A method of preparing homogeneously pure CAP37 using hydrophobic HPLC is described. Bioactive peptide fragments of CAP37 having chemotactic, antibacterial and/or LPS-binding activity are disclosed. Finally, methods of treating wounds, diseased tissue, such as tumors, and infections are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 95:92525 USPATFULL
TI Method of increasing monocyte chemotaxis with CAP37 and monocyte chemotactic portions thereof
IN Pereira, Heloise A., Decatur, GA, United States
Spitznagel, John K., Decatur, GA, United States
PA Emory University, Atlanta, GA, United States (U.S. corporation)
PI US 5458874 19951017
AI US 1992-969931 19921030 (7)
RLI Continuation of Ser. No. US 1992-855417, filed on 18 Mar 1992 which is a continuation-in-part of Ser. No. US 1990-543151, filed on 25 Jun 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-375739, filed on 5 Jul 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Furman, Keith C.
LREP Needle & Rosenberg
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 2618
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IN Pereira, Heloise A., Decatur, GA, United States
Spitznagel, John K., Decatur, GA, United States

L46 ANSWER 55 OF 306 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 6
SO BIOCONJUGATE CHEMISTRY, (SEP/OCT 1995) Vol. 6, No. 5, pp. 624-629.
ISSN: 1043-1802.
TI GENERATION OF A POTENT CHIMERIC TOXIN BY REPLACEMENT OF DOMAIN-III OF PSEUDOMONAS EXOTOXIN WITH RICIN-A CHAIN KDEL
AB Following cellular uptake, Pseudomonas exotoxin (PE) is **cleaved** by cellular **protease** which generates an enzymatically active C-terminal fragment (amino acids 280-613). This 37 kD fragment translocates to the cell cytosol where it ADP-ribosylates elongation factor 2 and inhibits protein synthesis. A **recombinant** hybrid toxin (designated PE-RTA) in which the ADP-ribosylation domain (domain III) was replaced by the RNA N-glycosidase domain of **ricin** (the A chain or RTA) has been produced in E. coli. The hybrid toxin effectively and specifically depurinated 28S ribosomal. RNA, indicating that the **ricin** A moiety folded into its native conformation. The cytotoxicity of PE-RTA for L929 cells was approximately 100-fold less than either native PE or whole **ricin**. However, the addition of the tetrapeptide KDEL to the C-terminus of PE-RTA (producing PE-RTA KDEL) increased cytotoxicity to the level of the native toxins. By analogy to PE, both PE-RTA and PE-RTA KDEL would be proteolytically **cleaved** within PE domain II during cell entry. A single amino acid substitution, believed to disrupt an essential step in the transport of the catalytically active PE fragment to the cell cytosol (Trp281 to Ala: Zdanovsky, A. G., Chiron, M., Pastan, I., and FitzGerald, D. J. (1993) J. Biol. Chem. 268, 21791-21799), reduced the cytotoxicities of both PE and PE-RTA KDEL by approximately 100-fold. Taken together, these data show that the **ricin** A chain component of the hybrid toxin requires essential PE-derived sequences at both the N- and C-termini of the translocating fragment. Clearly, in the context of this fusion protein, **ricin** A chain cannot effect its own transfer to the cytosol.
AN 95:706321 SCISEARCH
GA The Genuine Article (R) Number: RY634
TI GENERATION OF A POTENT CHIMERIC TOXIN BY REPLACEMENT OF DOMAIN-III OF PSEUDOMONAS EXOTOXIN WITH RICIN-A CHAIN KDEL
AU PITCHER C; ROBERTS L; FAWELL S; ZDANOVSKY A G; FITZGERALD D J (Reprint); LORD J M
CS NCI, DIV CANC BIOL DIAG & CTR, MOLEC BIOL LAB, BLDG 37, ROOM 4B03, 37 CONVENT DR MSC 4255, BETHESDA, MD, 20892 (Reprint); NCI, DIV CANC BIOL DIAG & CTR, MOLEC BIOL LAB, BETHESDA, MD, 20892; UNIV WARWICK, DEPT BIOL SCI, COVENTRY CV4 7AL, W MIDLANDS, ENGLAND; BIOGEN INC, CAMBRIDGE, MA, 02142
CYA USA; ENGLAND
SO BIOCONJUGATE CHEMISTRY, (SEP/OCT 1995) Vol. 6, No. 5, pp. 624-629.
ISSN: 1043-1802.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AU PITCHER C; ROBERTS L; FAWELL S; ZDANOVSKY A G; FITZGERALD D J (Reprint); LORD J M

L46 ANSWER 56 OF 306 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 7
SO BIOCONJUGATE CHEMISTRY, (NOV/DEC 1993) Vol. 4, No. 6, pp. 440-447.
ISSN: 1043-1802.
TI BIOLOGICALLY-ACTIVE INTERLEUKIN 2-RICIN A-CHAIN FUSION PROTEINS MAY REQUIRE INTRACELLULAR PROTEOLYTIC CLEAVAGE TO EXHIBIT A CYTOTOXIC EFFECT
AB DNA fusions encoding chimeric proteins in which human interleukin 2 (IL2) was fused to the A subunit of the plant cytotoxin **ricin** (RA) have been expressed in Xenopus oocytes. The constructs contained N-terminal IL2 and C-terminal RA, or N-terminal RA and C-terminal IL2. In the expressed chimeric proteins, the IL2 and RA moieties were joined by a

peptide sequence containing a proteolytic **cleavage** site. Two proteolytically-sensitive peptide sequences were utilized; a peptide that forms the trypsin-sensitive disulfide-bonded loop in diphtheria toxin (DT) or a synthetic peptide containing the factor Xa recognition site in a sequence flanked by two cysteine residues. In an in vitro cell free system the RA component was biologically active in all chimeric proteins produced since it specifically depurinated 28S ribosomal RNA. Proteolytic **cleavage** of the chimeras with either trypsin or factor Xa as appropriate separated the IL2 and RA moieties, but they did not remain covalently linked by a disulfide bond. Because of this, the cytotoxicity of **protease**-treated chimeras could not be assessed. Chimeras not pretreated with factor Xa but which contained the factor Xa target sequence were not cytotoxic to CTLL-2 cells. Rather, these molecules had a stimulatory effect that was ascribed to the IL2 moiety. In contrast, **recombinant** chimeric toxins containing the DT loop sequence were cytotoxic to CTLL-2 cells. Taken together the data suggest that RA-containing chimeras require intracellular proteolytic **cleavage** to release the RA moiety to render them cytotoxic to target cells.

AN 93:733659 SCISEARCH
GA The Genuine Article (R) Number: MK939
TI BIOLOGICALLY-ACTIVE INTERLEUKIN 2-RICIN A-CHAIN FUSION PROTEINS MAY REQUIRE INTRACELLULAR PROTEOLYTIC CLEAVAGE TO EXHIBIT A CYTOTOXIC EFFECT
AU COOK J P; SAVAGE P M; LORD J M; ROBERTS L M (Reprint)
CS UNIV WARWICK, DEPT BIOL SCI, COVENTRY CV4 7AL, W MIDLANDS, ENGLAND; HAMMERSMITH HOSP, IMPERIAL CANC RES FUND, CLIN ONCOL GRP, LONDON W12 0HS, ENGLAND
CYA ENGLAND
SO BIOCONJUGATE CHEMISTRY, (NOV/DEC 1993) Vol. 4, No. 6, pp. 440-447. ISSN: 1043-1802.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 28
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AU COOK J P; SAVAGE P M; LORD J M; ROBERTS L M (Reprint)

L46 ANSWER 57 OF 306 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 8
SO BIOCONJUGATE CHEMISTRY, (SEP/OCT 1992) Vol. 3, No. 5, pp. 375-381. ISSN: 1043-1802.
TI PREPARATION AND CHARACTERIZATION OF **RECOMBINANT** PRORICIN CONTAINING AN ALTERNATIVE PROTEASE-SENSITIVE LINKER SEQUENCE
AB The aim of this study was to determine the feasibility of utilizing a factor Xa-specific **cleavage** site within a **recombinant** protein containing the **ricin** A chain (RTA) sequence. Release of RTA is believed to be an essential step during the intracellular phase of **ricin** intoxication. Failure to incorporate such **cleavage** sites in fusions containing RTA results in a loss of toxin action (O'Hare, M., et al. (1990) FEBS Lett.273,200. Kim, J., and Weaver, R.F. (1988) Gene 68,315). In this report we describe the introduction of a factor Xa-specific site in the linker of proricin, which we use here as a model substrate. Upon purification of the **recombinant** mutant proricin after expression in Xenopus oocytes, we demonstrate that the **protease** does have access to the engineered recognition sequence (albeit at low efficiency) and that the presence of the latter does not interfere with disulfide bond formation or the lectin activity of the **ricin** B chain moiety. Upon **cleavage** and reduction, the RTA polypeptide displays ribosome-inactivating ability, indicating that the presence of the modified linker at its C-terminus does not interfere with its catalytic activity. The general applicability of using such a **cleavage** site in **recombinant** fusions with RTA is discussed.
AN 92:581073 SCISEARCH
GA The Genuine Article (R) Number: JQ428
TI PREPARATION AND CHARACTERIZATION OF **RECOMBINANT** PRORICIN CONTAINING AN ALTERNATIVE PROTEASE-SENSITIVE LINKER SEQUENCE

AU WESTBY M; ARGENT R H; PITCHER C; LORD J M; ROBERTS L M (Reprint)
CS UNIV WARWICK, DEPT BIOL SCI, COVENTRY CV4 7AL, W MIDLANDS, ENGLAND
CYA ENGLAND
SO BIOCONJUGATE CHEMISTRY, (SEP/OCT 1992) Vol. 3, No. 5, pp. 375-381.
ISSN: 1043-1802.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AU WESTBY M; ARGENT R H; PITCHER C; LORD J M; ROBERTS L M (Reprint)

L46 ANSWER 58 OF 306 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 9
SO J IMMUNOL, (1982) 128 (6), 2682-2690.
CODEN: JOIMA3. ISSN: 0022-1767.
TI TENTATIVE ASSIGNMENT OF ALLELES FOR GUINEA-PIG IA ANTIGENS 1. IA.3 5 AND IA.4 5 SHARE STRUCTURAL HOMOLOGY EXPECTED FOR ALLELES.
AB Although the guinea pig has served as an important model in the investigation of Ir gene-controlled immune response, characterization of the I region of the guinea pig major histocompatibility complex was hindered by the lack of I region **recombinant** strains. A rigorous chemical examination of guinea pig Ia molecules was undertaken to gather structural data that might lead to a tentative assignment of alleles in the guinea pig I region. Three Ia molecules were examined in this study:Ia.2 and Ia.4,5 from strain 2 animals and Ia.3,5 from strain 13 (and DHCBA) animals. 3H-leucine-labeled antigens were purified by **ricin** affinity chromatography and indirect immunoprecipitation with specific alloantisera. Isolated .alpha.- and .beta.-chains of the Ia molecules were subjected to several chemical manipulations. Initial examination of the 3 Ia molecules by isoelectric focusing demonstrated that the .alpha.- and .beta.-chains of the Ia.3,5 and Ia.4,5 molecules focused with highly similar isoelectric points; the .alpha.- and .beta.-chains, respectively, of Ia.2 focused in a more acidic region than their counterparts from Ia.3,5. Analysis of the purified chains by CNBr **cleavage** and Staphylococcal **protease** V-8 digestion demonstrated similar sized fragments from the respective chains Ia.3,5 and Ia.4,5, but different fragments from the chains of Ia.2. Peptide mapping by high pressure liquid chromatography after trypsin/chymotrypsin **cleavage** demonstrated that the Ia.3,5 .alpha.-chain shared 47% of its peptides with the Ia.4,5 .alpha.-chain, but only 22% of its peptides with the Ia.2 .alpha.-chain. The Ia.3,5 and Ia.4,5 .beta.-chains shared 68% of their peptides while the Ia.3,5 and Ia.2 .beta.-chains shared only 49% of their peptides. This degree of similarity is consistent with the findings in the mouse H-2 system for alleles at the same locus. Ia.3,5 and Ia.4,5 molecules apparently are the products of alleles at the Ia .alpha.- and .beta.-loci, at least 1 of which is contained within the I region of the guinea pig major histocompatibility complex.
AN 1982:310500 BIOSIS
DN BA74:82980
TI TENTATIVE ASSIGNMENT OF ALLELES FOR GUINEA-PIG IA ANTIGENS 1. IA.3 5 AND IA.4 5 SHARE STRUCTURAL HOMOLOGY EXPECTED FOR ALLELES.
AU ABRUZZINI L N K F; SCHWARTZ B D
CS DEP. MED., DIV. RHEUMATOL., HOWARD HUGHES MED. INST. LAB., WASHINGTON UNIV. MED., ST. LOUIS, MO. 63110, USA.
SO J IMMUNOL, (1982) 128 (6), 2682-2690.
CODEN: JOIMA3. ISSN: 0022-1767.
FS BA; OLD
LA English
AU ABRUZZINI L N K F; SCHWARTZ B D

L46 ANSWER 59 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
AN AAG66985 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66985 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP325 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 60 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66984 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66984 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin

linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP324 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 61 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66983 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66983 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP323 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 62 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66982 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**

-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAG66982 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP322 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 63 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66981 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66981 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP321 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 64 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66980 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66980 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP320 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 65 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66979 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells

expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAG66979 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP318 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 66 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66978 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66978 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004

US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP316 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 67 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66977 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66977 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP315 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 68 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66976 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or

cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAG66976 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP314 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 69 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66975 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66975 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP313 (UPA).
IN Braun C; Purac A; Borgford T

L46 ANSWER 70 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66974 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66974 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP309 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 71 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66973 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders

and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAG66973 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP308 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 72 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66972 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66972 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP305 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 73 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66971 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAG66971 Peptide DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin linker region of PAP304 (MMP-9).

IN Braun C; Purac A; Borgford T

L46 ANSWER 74 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66970 Peptide DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9

(MMP-9) or UPA.
AN AAG66970 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP303 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 75 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66969 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66969 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP302 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 76 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAG66968 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linkers generated from the wild type preproricin linker. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAG66968 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin linker region of PAP301 (MMP-9).
IN Braun C; Purac A; Borgford T

L46 ANSWER 77 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAG66967 Peptide DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is the wild type preproricin linker sequence.
AN AAG66967 Peptide DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant wild type ricin linker peptide.
IN Braun C; Purac A; Borgford T

L46 ANSWER 78 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94411 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.
AN AAW94411 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-213 and pAP-214.
IN Borgford T

L46 ANSWER 79 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94419 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific

protease (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Plasmodium falciparum **protease**- sensitive linker from the present invention.

AN AAW94419 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum protease-sensitive linker pAP-225 and pAP-226.
IN Borgford T

L46 ANSWER 80 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94433 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Candida aspartic **protease**-sensitive linker from the present invention.

AN AAW94433 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Candida aspartic protease-sensitive linker pAP-259 and pAP-260.
IN Borgford T

L46 ANSWER 81 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94437 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94437 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for HCV-B, pAP-264.
IN Borgford T

L46 ANSWER 82 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94432 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94432 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Viral protease-sensitive linker pAP-257 and pAP-258.

IN Borgford T

L46 ANSWER 83 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94431 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further

improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94431 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-255 and pAP-256.
IN Borgford T

L46 ANSWER 84 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94430 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94430 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-253 and pAP-254.
IN Borgford T

L46 ANSWER 85 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94429 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.
AN AAW94429 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-239 and pAP-240.
IN Borgford T

L46 ANSWER 86 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94428 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for

(III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94428 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-237 and pAP-238.
IN Borgford T

L46 ANSWER 87 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94427 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94427 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent

LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-247 and pAP-248.
IN Borgford T

L46 ANSWER 88 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94426 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.
AN AAW94426 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-245 and pAP-246.
IN Borgford T

L46 ANSWER 89 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94425 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary,

pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.

AN AAW94425 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-249 and pAP-250.
IN Borgford T

L46 ANSWER 90 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94424 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.
AN AAW94424 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-235 and pAP-236.
IN Borgford T

L46 ANSWER 91 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94423 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed viral **protease**-sensitive linker from the present invention.
AN AAW94423 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Viral protease-sensitive linker pAP-233 and pAP-234.
IN Borgford T

L46 ANSWER 92 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94436 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus

transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94436 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for HCV-A, pAP-262.
IN Borgford T

L46 ANSWER 93 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94422 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Plasmodium falciparum **protease**- sensitive linker from the present invention.
AN AAW94422 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain

linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum protease-sensitive linker pAP-231 and pAP-232.
IN Borgford T

L46 ANSWER 94 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94421 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Plasmodium falciparum **protease**- sensitive linker from the present invention.
AN AAW94421 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum protease-sensitive linker pAP-229 and pAP-230.
IN Borgford T

L46 ANSWER 95 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94420 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids

(I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Plasmodium falciparum **protease**- sensitive linker from the present invention.

AN AAW94420 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Plasmodium falciparum protease-sensitive linker pAP-227 and pAP-228.

IN Borgford T

L46 ANSWER 96 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94451 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs

only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94451 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for kallikrein, pAP-292.

IN Borgford T

L46 ANSWER 97 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94450 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94450 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for prostate-specific antigen, pAP290.

IN Borgford T

L46 ANSWER 98 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased

cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94449 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94449 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for tissue-type plasminogen A, pAP-288.
IN Borgford T

L46 ANSWER 99 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94448 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses

exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94448 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for MMP-13, pAP-286.
IN Borgford T

L46 ANSWER 100 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94447 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94447 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for MMP-11, pAP-284.
IN Borgford T

L46 ANSWER 101 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94446 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94446 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for MT-MMP, pAP-282.
IN Borgford T

L46 ANSWER 102 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94445 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells,

transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94445 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for urokinase-like PA, pAP-280.

IN Borgford T

L46 ANSWER 103 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94444 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94444 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for MMP-1, pAP-278.

IN Borgford T

L46 ANSWER 104 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94443 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94443 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for Cathepsin D, pAP-276.
IN Borgford T

L46 ANSWER 105 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94442 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for

(III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94442 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for Cathepsin L, pAP-274.

IN Borgford T

L46 ANSWER 106 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94441 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94441 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for Cathepsin B, pAP-272.
IN Borgford T

L46 ANSWER 107 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94440 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94440 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for MMP-2, pAP-270.
IN Borgford T

L46 ANSWER 108 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94439 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella

zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94439 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Mutant proproricin linker region for HCV-D, pAP-268.

IN Borgford T

L46 ANSWER 109 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAW94438 peptide DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.

AN AAW94438 peptide DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for HCV-C, pAP-266.
IN Borgford T

L46 ANSWER 110 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94435 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Candida aspartic **protease**-sensitive linker from the present invention.
AN AAW94435 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Candida aspartic protease-sensitive linker pAP-263 and pAP-264.
IN Borgford T

L46 ANSWER 111 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94434 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary,

pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Candida aspartic **protease**-sensitive linker from the present invention.

AN AAW94434 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Candida aspartic protease-sensitive linker pAP-261 and pAP-262.
IN Borgford T

L46 ANSWER 112 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94453 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94453 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for calpain, pAP-296.
IN Borgford T

L46 ANSWER 113 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94452 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed mutant preproricin linker from the present invention.
AN AAW94452 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Mutant proproricin linker region for neutrophil elastase, pAP-294.
IN Borgford T

L46 ANSWER 114 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94454 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified

linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a linker sequence from the present invention.

AN AAW94454 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Wild-type linker region.
IN Borgford T

L46 ANSWER 115 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94412 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.

AN AAW94412 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-215 and pAP-216.
IN Borgford T

L46 ANSWER 116 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94417 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.
AN AAW94417 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-243 and pAP-244.
IN Borgford T

L46 ANSWER 117 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94416 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and

including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.

AN AAW94416 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-241 and pAP-242.
IN Borgford T

L46 ANSWER 118 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94415 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the

present invention.
AN AAW94415 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-221 and pAP-222.
IN Borgford T

L46 ANSWER 119 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94414 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.
AN AAW94414 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-219 and pAP-220.
IN Borgford T

L46 ANSWER 120 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased

cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94413 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed cancer **protease**-sensitive amino acid linker from the present invention.
AN AAW94413 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cancer protease-sensitive amino acid linker pAP-217 and pAP-218.
IN Borgford T

L46 ANSWER 121 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAW94418 peptide DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde

translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed Plasmodium falciparum **protease**- sensitive linker from the present invention.

AN AAW94418 peptide DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum protease-sensitive linker pAP-223 and pAP-224.
IN Borgford T

L46 ANSWER 122 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAW36886 Peptide DGENE
AB This claimed peptide is a **cleavage** recognition site for a HTLV-I **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97919) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.
AN AAW36886 Peptide DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC HTLV-II protease cleavage recognition site.
IN Borgford T

L46 ANSWER 123 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAW36885 Peptide DGENE

AB This claimed peptide is a **cleavage** recognition site for a HTLV-I **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97916) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.

AN AAW36885 Peptide DGENE

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

IN Borgford T

PA (CANG-N) CANGENE CORP.

PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429

PRAI US 1996-16509 19960430

DT Patent

LA English

OS 1997-549735 [50]

DESC HTLV-II protease cleavage recognition site.

IN Borgford T

L46 ANSWER 124 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

AN AAW36884 Peptide DGENE

AB This claimed peptide is a **cleavage** recognition site for a HTLV-I **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97913) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.

AN AAW36884 Peptide DGENE

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

IN Borgford T

PA (CANG-N) CANGENE CORP.

PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429

PRAI US 1996-16509 19960430

DT Patent
LA English
OS 1997-549735 [50]
DESC HTLV-I protease cleavage recognition site.
IN Borgford T

L46 ANSWER 125 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAW36883 Peptide DGENE
AB This claimed peptide is a **cleavage** recognition site for a HTLV-I **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97910) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.
AN AAW36883 Peptide DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC HTLV-I protease cleavage recognition site.
IN Borgford T

L46 ANSWER 126 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAW36882 Peptide DGENE
AB This claimed peptide is a **cleavage** recognition site for a HIV **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97901) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**,

and thus can be used to specifically target infected cells without the need for a cell binding component.

AN AAW36882 Peptide DGENE

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

IN Borgford T

PA (CANG-N) CANGENE CORP.

PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429

PRAI US 1996-16509 19960430

DT Patent

LA English

OS 1997-549735 [50]

DESC HIV protease cleavage recognition site.

IN Borgford T

L46 ANSWER 127 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

AN AAW36881 Peptide DGENE

AB This claimed peptide is a **cleavage** recognition site for a HIV **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97900) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.

AN AAW36881 Peptide DGENE

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

IN Borgford T

PA (CANG-N) CANGENE CORP.

PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429

PRAI US 1996-16509 19960430

DT Patent

LA English

OS 1997-549735 [50]

DESC HIV protease cleavage recognition site.

IN Borgford T

L46 ANSWER 128 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus

AN AAW36880 Peptide DGENE

AB This claimed peptide is a **cleavage** recognition site for a HIV **protease**. It is utilised as a linker between the A and B chains of a **ricin**-like protein in a novel **recombinant** protein. A nucleic acid (see AAT97899) encoding such a construct is obtained by PCR mutagenesis of the wild-type **ricin** linker

sequence. The invention provides novel **recombinant** proteins which incorporate the A and B chains of a **ricin**-like toxin (preferably the A and B chains of **ricin**) linked by a heterologous linker sequence containing a **cleavage** recognition site for a retroviral **protease** such as HIV **protease** (see AAW36880-82), HTLV-I (see AAW36883-43) or HTLV-II (see AAW36885-65). The **recombinant** proteins selectively inhibit or destroy mammalian cells infected with a retrovirus such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by a retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.

AN AAW36880 Peptide DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC HIV protease cleavage recognition site.
IN Borgford T

L46 ANSWER 129 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79940 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79940 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent

LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP325 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 130 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79939 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79939 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 325-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 131 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79938 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders

and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79938 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 325-3'.

IN Braun C; Purac A; Borgford T

L46 ANSWER 132 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79937 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79937 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP324 nucleotide sequence.

IN Braun C; Purac A; Borgford T

L46 ANSWER 133 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79936 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79936 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP324 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 134 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79935 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79935 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 324-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 135 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79934 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79934 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 324-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 136 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79933 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T-

and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79933 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP323 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 137 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79932 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79932 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English

OS 2001-300164 [31]
DESC Mutant preproricin pAP323 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 138 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79931 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79931 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 323-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 139 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79930 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The

present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79930 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 323-3'.

IN Braun C; Purac A; Borgford T

L46 ANSWER 140 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79929 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79929 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP322 nucleotide sequence.

IN Braun C; Purac A; Borgford T

L46 ANSWER 141 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79928 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79928 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP322 UPA variant linker region DNA.

IN Braun C; Purac A; Borgford T

L46 ANSWER 142 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79927 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79927 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 322-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 143 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79926 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79926 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 322-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 144 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79925 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic

cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79925 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP321 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 145 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79924 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79924 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]

DESC Mutant preproricin pAP321 UPA variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 146 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79923 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79923 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 321-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 147 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79922 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker

sequence using the wild type preproricin linker sequence as a template.
AN AAI79922 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 321-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 148 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79921 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAI79921 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP320 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 149 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79920 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A

chain of a **ricin**-like toxin, a B chain of a **ricin**
-like toxin and a heterologous linker that links the A and B chains. The
linker sequence contains a **cleavage** recognition site for a
specific **protease** such as those found in inflammatory cells and
cancer cells. The protein is useful for inhibiting or destroying cells
expressing a specific **protease**, e.g. cancer cells found in T-
and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic
cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal
cancer, breast cancer, prostate cancer or non-small cell lung cancer, or
cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or
central nervous system disease. The protein is useful for treating cancer
and inflammation. The protein has the specificity for cells that contain
a specific **protease**, including those of inflammatory disorders
and cancer cells, without the need for a cell binding component. The
present sequence is one of a number of variant linker regions generated
from the wild type preproricin linker region. The variant linkers contain
a **cleavage** recognition site for either matrix metalloproteinase
9 (MMP-9) or UPA.

AN AAI79920 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin
linked by a novel linker sequence that is specifically **cleaved**
and activated by **protease** specific to cancer is useful for
treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP320 UPA variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 150 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin
linked by a novel linker sequence that is specifically **cleaved**
and activated by **protease** specific to cancer is useful for
treating inflammation and cancer -
AN AAI79919 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A
chain of a **ricin**-like toxin, a B chain of a **ricin**
-like toxin and a heterologous linker that links the A and B chains. The
linker sequence contains a **cleavage** recognition site for a
specific **protease** such as those found in inflammatory cells and
cancer cells. The protein is useful for inhibiting or destroying cells
expressing a specific **protease**, e.g. cancer cells found in T-
and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic
cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal
cancer, breast cancer, prostate cancer or non-small cell lung cancer, or
cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or
central nervous system disease. The protein is useful for treating cancer
and inflammation. The protein has the specificity for cells that contain
a specific **protease**, including those of inflammatory disorders
and cancer cells, without the need for a cell binding component. The
present sequence is a mutagenic primer used to generate a variant linker
sequence using the wild type preproricin linker sequence as a template.
AN AAI79919 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin
linked by a novel linker sequence that is specifically **cleaved**
and activated by **protease** specific to cancer is useful for
treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 320-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 151 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79918 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79918 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 320-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 152 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79917 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal

cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79917 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP318 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 153 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79916 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79916 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP318 MMP-9 variant linker region DNA.

IN Braun C; Purac A; Borgford T

L46 ANSWER 154 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79915 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79915 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 318-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 155 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79914 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79914 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 318-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 156 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79913 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAI79913 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP316 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 157 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79912 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**

-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79912 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP316 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 158 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79911 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79911 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 316-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 159 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79910 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79910 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 316-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 160 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79909 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or

cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79909 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP315 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 161 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79908 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79908 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP315 UPA variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 162 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79907 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79907 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 315-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 163 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79906 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79906 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 315-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 164 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79905 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAI79905 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP314 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 165 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79904 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The

linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79904 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP314 UPA variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 166 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79903 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79903 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 314-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 167 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79902 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79902 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 314-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 168 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79901 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or

central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79901 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP313 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 169 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79900 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79900 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP313 UPA variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 170 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79899 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79899 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 313-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 171 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79898 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79898 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin

linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 313-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 172 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79897 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAI79897 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP309 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 173 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79896 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a

specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79896 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP309 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 174 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79895 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79895 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004

US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 309-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 175 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79894 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79894 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 309-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 176 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79893 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer

and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is the linker region of the wild type preproricin coding sequence.

AN AAI79893 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 177 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79892 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAI79892 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP308 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 178 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79891 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79891 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP308 MMP-9 variant linker region DNA.

IN Braun C; Purac A; Borgford T

L46 ANSWER 179 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79890 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79890 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved**

and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 308-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 180 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79889 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79889 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 308-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 181 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79888 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and

cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79888 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP305 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 182 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79887 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79887 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP305 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 183 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79886 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79886 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 305-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 184 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79885 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain

a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79885 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 305-3'.

IN Braun C; Purac A; Borgford T

L46 ANSWER 185 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79884 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79884 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP304 nucleotide sequence.

IN Braun C; Purac A; Borgford T

L46 ANSWER 186 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
AN AAI79883 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79883 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP304 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 187 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79882 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin**-like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79882 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for

treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 304-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 188 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79881 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79881 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 304-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 189 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79880 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells

expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79880 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP303 nucleotide sequence.

IN Braun C; Purac A; Borgford T

L46 ANSWER 190 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79879 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.

AN AAI79879 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP303 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 191 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79878 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79878 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 303-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 192 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79877 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders

and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79877 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 303-3'.

IN Braun C; Purac A; Borgford T

L46 ANSWER 193 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79876 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79876 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Mutant preproricin pAP302 nucleotide sequence.

IN Braun C; Purac A; Borgford T

L46 ANSWER 194 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79875 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79875 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP302 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 195 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79874 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79874 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 302-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 196 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79873 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79873 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 302-3'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 197 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79872 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T-

and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.

AN AAI79872 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP301 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 198 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79871 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is one of a number of variant linker regions generated from the wild type preproricin linker region. The variant linkers contain a **cleavage** recognition site for either matrix metalloproteinase 9 (MMP-9) or UPA.
AN AAI79871 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English

OS 2001-300164 [31]
DESC Mutant preproricin pAP301 MMP-9 variant linker region DNA.
IN Braun C; Purac A; Borgford T

L46 ANSWER 199 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79870 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.
AN AAI79870 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor oil plant preproricin linker mutagenic primer 301-5'.
IN Braun C; Purac A; Borgford T

L46 ANSWER 200 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAI79869 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The

present sequence is a mutagenic primer used to generate a variant linker sequence using the wild type preproricin linker sequence as a template.

AN AAI79869 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker mutagenic primer 301-3'.

IN Braun C; Purac A; Borgford T

L46 ANSWER 201 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAI79868 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is the linker region of the wild type preproricin coding sequence.

AN AAI79868 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor oil plant preproricin linker region DNA.

IN Braun C; Purac A; Borgford T

L46 ANSWER 202 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAH77626 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a primer used in the production of variants of the castor bean plant preproricin linker.

AN AAH77626 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004

PRAI US 1999-157807 19991004
US 2000-197409 20000414

DT Patent

LA English

OS 2001-300164 [31]

DESC Castor bean plant preproricin Ricin1729PstI primer.

IN Braun C; Purac A; Borgford T

L46 ANSWER 203 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

AN AAH77625 DNA DGENE

AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a primer used in the production of variants of the castor bean plant preproricin linker.

AN AAH77625 DNA DGENE

TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -

IN Braun C; Purac A; Borgford T

PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.

PI WO 2001025267 A2 20010412 146p

AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor bean plant preproricin Ricin109-Eco primer.
IN Braun C; Purac A; Borgford T

L46 ANSWER 204 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAH77624 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a primer used to amplify castor bean plant preproricin cDNA.
AN AAH77624 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor bean plant preproricin cDNA upstream primer Ricin-99.
IN Braun C; Purac A; Borgford T

L46 ANSWER 205 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAH77623 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or

cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence is a primer used to generate castor bean plant preproricin cDNA from total RNA.

AN AAH77623 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Castor bean plant preproricin RNA RT primer Ricin1729C.
IN Braun C; Purac A; Borgford T

L46 ANSWER 206 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
AN AAH77622 DNA DGENE
AB The invention relates to a **recombinant** protein comprising an A chain of a **ricin**-like toxin, a B chain of a **ricin** -like toxin and a heterologous linker that links the A and B chains. The linker sequence contains a **cleavage** recognition site for a specific **protease** such as those found in inflammatory cells and cancer cells. The protein is useful for inhibiting or destroying cells expressing a specific **protease**, e.g. cancer cells found in T- and B-cell lymphoproliferative diseases, ovarian cancer, pancreatic cancer, head and neck cancer, squamous cell carcinoma, gastrointestinal cancer, breast cancer, prostate cancer or non-small cell lung cancer, or cells found in rheumatoid arthritis, atherosclerosis, Crohn's disease or central nervous system disease. The protein is useful for treating cancer and inflammation. The protein has the specificity for cells that contain a specific **protease**, including those of inflammatory disorders and cancer cells, without the need for a cell binding component. The present sequence encodes a **recombinant** protein of the invention.
AN AAH77622 DNA DGENE
TI New proteins comprising A and B chains of **ricin**-like toxin linked by a novel linker sequence that is specifically **cleaved** and activated by **protease** specific to cancer is useful for treating inflammation and cancer -
IN Braun C; Purac A; Borgford T
PA (TWIN-N) TWINSTRAND THERAPEUTICS INC.
PI WO 2001025267 A2 20010412 146p
AI WO 2000-CA1162 20001004
PRAI US 1999-157807 19991004
US 2000-197409 20000414
DT Patent
LA English
OS 2001-300164 [31]
DESC Mutant preproricin pAP325 nucleotide sequence.
IN Braun C; Purac A; Borgford T

L46 ANSWER 207 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04248 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04248 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-296 insert DNA sequence.

IN Borgford T

L46 ANSWER 208 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04247 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells,

transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04247 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-294 insert DNA sequence.
IN Borgford T

L46 ANSWER 209 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04246 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04246 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-292 insert DNA sequence.
IN Borgford T

L46 ANSWER 210 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04245 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04245 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-290 insert DNA sequence.
IN Borgford T

L46 ANSWER 211 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04244 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for

(III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04244 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-288 insert DNA sequence.

IN Borgford T

L46 ANSWER 212 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04243 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04243 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-286 insert DNA sequence.
IN Borgford T

L46 ANSWER 213 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04242 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04242 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-284 insert DNA sequence.
IN Borgford T

L46 ANSWER 214 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04241 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella

zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04241 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-282 insert DNA sequence.
IN Borgford T

L46 ANSWER 215 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04240 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04240 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent

LA English
OS 1999-009431 [01]
DESC pAP-280 insert DNA sequence.
IN Borgford T

L46 ANSWER 216 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04239 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04239 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-278 insert DNA sequence.
IN Borgford T

L46 ANSWER 217 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04238 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi,

parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04238 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-276 insert DNA sequence.

IN Borgford T

L46 ANSWER 218 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04237 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04237 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029

US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-274 insert DNA sequence.
IN Borgford T

L46 ANSWER 219 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04236 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04236 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-272 insert DNA sequence.
IN Borgford T

L46 ANSWER 220 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04235 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for

treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04235 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-270 insert DNA sequence.

IN Borgford T

L46 ANSWER 221 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04262 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04262 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HSV-A linker regions of pAP-233.
IN Borgford T

L46 ANSWER 222 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04261 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04261 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum-E linker regions of pAP-231.
IN Borgford T

L46 ANSWER 223 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04260 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified

linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04260 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC Plasmodium falciparum-D linker regions of pAP-229.

IN Borgford T

L46 ANSWER 224 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04259 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04259 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum-C linker regions of pAP-227.
IN Borgford T

L46 ANSWER 225 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04258 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04258 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum-B linker regions of pAP-225.
IN Borgford T

L46 ANSWER 226 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04257 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus

transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04257 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Plasmodium falciparum-A linker regions of pAP-223.
IN Borgford T

L46 ANSWER 227 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04256 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04256 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased

cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Thermolysin-like MMP linker regions of pAP-221.
IN Borgford T

L46 ANSWER 228 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04255 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04255 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-9 linker regions of pAP-219.
IN Borgford T

L46 ANSWER 229 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04254 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and

including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04254 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC MMP-7 linker regions of pAP-217.

IN Borgford T

L46 ANSWER 230 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04253 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04253 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-3 linker regions of pAP-215.
IN Borgford T

L46 ANSWER 231 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04252 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04252 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cathepsin B linker regions of pAP-213.
IN Borgford T

L46 ANSWER 232 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04251 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids

(I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04251 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Baculovirus transfer vector pVL1393 DNA sequence.
IN Borgford T

L46 ANSWER 233 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04250 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a PCR primer from

the present invention.
AN AAX04250 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Proricin production and cloning linker variant PCR primer Ricin1729PstI.
IN Borgford T

L46 ANSWER 234 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04249 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a PCR primer from the present invention.
AN AAX04249 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Proricin production and cloning linker variant PCR primer Ricin-109Eco.
IN Borgford T

L46 ANSWER 235 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04278 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04278 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029

US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC HCV-D linker regions of pAP-268.

IN Borgford T

L46 ANSWER 236 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04277 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further

improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04277 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HCV-C linker regions of pAP-266.
IN Borgford T

L46 ANSWER 237 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04276 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04276 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HCV-B linker regions of pAP-264.
IN Borgford T

L46 ANSWER 238 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain

linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04275 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04275 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC HCV-A linker regions of pAP-262.

IN Borgford T

L46 ANSWER 239 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04274 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde

translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04274 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC CAN linker regions of pAP-259.
IN Borgford T

L46 ANSWER 240 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04273 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04273 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HAV-B linker regions of pAP-255.
IN Borgford T

L46 ANSWER 241 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04272 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04272 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HAV-A linker regions of pAP-257.
IN Borgford T

L46 ANSWER 242 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04271 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a

cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04271 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC ILV linker regions of pAP-253.
IN Borgford T

L46 ANSWER 243 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04270 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04270 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HHV-6 linker regions of pAP-249.

IN Borgford T

L46 ANSWER 244 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04269 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04269 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC CMV-B linker regions of pAP-247.
IN Borgford T

L46 ANSWER 245 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04268 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I)

is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04268 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC CMV-A linker regions of pAP-245.
IN Borgford T

L46 ANSWER 246 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04267 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04267 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English

OS 1999-009431 [01]
DESC EBV-B linker regions of pAP-243.
IN Borgford T

L46 ANSWER 247 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04266 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04266 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC EBV-A linker regions of pAP-241.
IN Borgford T

L46 ANSWER 248 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04265 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes,

hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04265 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC VZV-B linker regions of pAP-239.
IN Borgford T

L46 ANSWER 249 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04264 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04264 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent
LA English
OS 1999-009431 [01]
DESC VZV-A linker regions of pAP-237.
IN Borgford T

L46 ANSWER 250 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04263 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04263 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC HSV-B linker regions of pAP-235.
IN Borgford T

L46 ANSWER 251 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04292 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary,

pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04292 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Calpain linker regions of pAP-296.
IN Borgford T

L46 ANSWER 252 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04291 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04291 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Neutrophil elastase linker regions of pAP-294.
IN Borgford T

L46 ANSWER 253 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04290 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04290 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Kallikrein linker regions of pAP-292.
IN Borgford T

L46 ANSWER 254 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04289 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to

inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04289 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Human prostate-specific antigen linker regions of pAP-290.
IN Borgford T

L46 ANSWER 255 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04288 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04288 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Tissue-type plasminogen activator linker regions of pAP-288.
IN Borgford T

L46 ANSWER 256 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04287 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04287 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-13 linker regions of pAP-286.
IN Borgford T

L46 ANSWER 257 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04286 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein

(IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04286 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-11 linker regions of pAP-284.
IN Borgford T

L46 ANSWER 258 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04285 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04285 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MT-MMP linker regions of pAP-282.
IN Borgford T

L46 ANSWER 259 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04284 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04284 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Urokinase-type plasminogen activator linker regions of pAP-280.
IN Borgford T

L46 ANSWER 260 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04283 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific

protease (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04283 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-1 linker regions of pAP-278.
IN Borgford T

L46 ANSWER 261 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04282 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04282 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain

linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cathepsin D linker regions of pAP-276.
IN Borgford T

L46 ANSWER 262 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04281 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.
AN AAX04281 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cathepsin L linker regions of pAP-274.
IN Borgford T

L46 ANSWER 263 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04280 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin

(II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04280 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cathepsin B linker regions of pAP-272.
IN Borgford T

L46 ANSWER 264 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04279 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a nucleotide sequence from the present invention.

AN AAX04279 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC MMP-2 linker regions of pAP-270.
IN Borgford T

L46 ANSWER 265 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04208 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04208 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC Cathepsin B linker regions of pAP-213 nucleotide sequence.
IN Borgford T

L46 ANSWER 266 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04219 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04219 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-236 insert containing ricin and the HSV-B linker.

IN Borgford T

L46 ANSWER 267 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04218 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs

only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04218 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029

US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-234 insert containing ricin and the HSV-A linker.

IN Borgford T

L46 ANSWER 268 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04217 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04217 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029

US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-232 insert containing ricin and the Plasmodium falciparum E linker.

IN Borgford T

L46 ANSWER 269 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased

cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04216 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04216 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-230 insert containing ricin and the Plasmodium falciparum D linker.
IN Borgford T

L46 ANSWER 270 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04215 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses

exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04215 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-228 insert containing ricin and the Plasmodium falciparum C linker.
IN Borgford T

L46 ANSWER 271 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04214 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04214 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-226 insert containing ricin and the Plasmodium falciparum B linker.
IN Borgford T

L46 ANSWER 272 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04213 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04213 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-224 insert containing ricin and the Plasmodium falciparum A linker.

IN Borgford T

L46 ANSWER 273 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04212 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells,

transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04212 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-222 insert containing ricin and the thermolysin-like MMP linker.
IN Borgford T

L46 ANSWER 274 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04211 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04211 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-220 insert containing ricin and the MMP-9 linker DNA sequence.
IN Borgford T

L46 ANSWER 275 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04210 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04210 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-218 insert containing ricin and the MMP-7 linker DNA sequence.
IN Borgford T

L46 ANSWER 276 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04209 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for

(III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04209 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-216 insert containing ricin and the MMP-3 linker DNA sequence.
IN Borgford T

L46 ANSWER 277 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04234 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04234 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]

DESC pAP-268 insert DNA sequence.
IN Borgford T

L46 ANSWER 278 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04233 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04233 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-266 insert DNA sequence.
IN Borgford T

L46 ANSWER 279 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells .
AN AAX04232 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella

zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04232 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-264 insert DNA sequence.
IN Borgford T

L46 ANSWER 280 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04231 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04231 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent

LA English
OS 1999-009431 [01]
DESC pAP-262 insert DNA sequence.
IN Borgford T

L46 ANSWER 281 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04230 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04230 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01].
DESC pAP-260 insert containing ricin and the CAN linker.
IN Borgford T

L46 ANSWER 282 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04229 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi,

parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04229 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-256 insert containing ricin and the HAV-B linker.
IN Borgford T

L46 ANSWER 283 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04228 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04228 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029

US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-258 insert containing ricin and the HAV-A linker.
IN Borgford T

L46 ANSWER 284 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04227 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04227 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-254 insert containing ricin and the ILV linker.
IN Borgford T

L46 ANSWER 285 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04226 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for

treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04226 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430

PRAI US 1997-63715 19971029
US 1997-45148 19970430

DT Patent

LA English

OS 1999-009431 [01]

DESC pAP-250 insert containing ricin and the HHV-6 linker.

IN Borgford T

L46 ANSWER 286 OF 306 DGENE (C) 2003 THOMSON DERWENT

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

AN AAX04225 DNA DGENE

AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04225 DNA DGENE

TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells

IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.

PI WO 9849311 A2 19981105 352p

AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-248 insert containing ricin and the CMV-B linker.
IN Borgford T

L46 ANSWER 287 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04224 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04224 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-246 insert containing ricin and the CMV-A linker.
IN Borgford T

L46 ANSWER 288 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04223 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified

linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04223 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-244 insert containing ricin and the EBV-B linker.
IN Borgford T

L46 ANSWER 289 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04221 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04221 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T

PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-240 insert containing ricin and the VZV-B linker.
IN Borgford T

L46 ANSWER 290 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04222 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.
AN AAX04222 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-242 insert containing ricin and the EBV-A linker.
IN Borgford T

L46 ANSWER 291 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
AN AAX04220 DNA DGENE
AB The present invention describes new purified and isolated nucleic acids (I) encoding: (i) the A and B chains of a **ricin**-like toxin (II); and (ii) a heterologous linker, joining the two chains and including a **cleavage** recognition site for a disease-specific **protease** (III). Also described are: (1) plasmids or baculovirus

transfer vectors that contain (I); and (2) **recombinant** protein (IV) consisting of the A and B chains of (II) joined by the specified linker. (IV), produced by expression of (I) in host cells, are used to inhibit or kill diseased cells that produce (III), particularly for treating cancers (e.g. leucocyte proliferation; cancer of ovary, pancreas, breast or prostate; glioma) or infections caused by fungi, parasites (e.g. malaria) or viruses (e.g. cytomegalovirus (CMV), herpes, hepatitis, rhinovirus, laryngeotracheitis, poliomyelitis or varicella zoster), also cystic fibrosis and multiple sclerosis. Alternatively, (I) is used to express (IV) in vivo. (IV) is toxic specifically for (III)-expressing cells and does not depend for specificity on a cell-binding component. When used to treat virus- infected cells, transcytosis and cytotoxicity of (IV) are increased by retrograde translocation from endoplasmic reticulum to cytoplasm (which some viruses exploit to avoid immune detection), so selectivity and safety are further improved. (IV) are not toxic until chain A is released and this occurs only in target cells. The present sequence represents a specifically claimed nucleic acid sequence from the present invention.

AN AAX04220 DNA DGENE
TI New nucleic acid encoding **ricin**-like toxin with an interchain linker **cleaved** by **protease** - is specific for diseased cells, useful for, e.g. killing selectively cancer or infected cells
IN Borgford T
PA (DNOV-N) DE NOVO ENZYME CORP.
PI WO 9849311 A2 19981105 352p
AI WO 1998-CA394 19980430
PRAI US 1997-63715 19971029
US 1997-45148 19970430
DT Patent
LA English
OS 1999-009431 [01]
DESC pAP-238 insert containing ricin and the VZV-A linker.
IN Borgford T

L46 ANSWER 292 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97901 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-190. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36882) that contains a **cleavage** site for HIV **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA and subcloning of the mutant DNA into vector pSB2. **Recombinant** baculovirus was obtained and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HIV. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97901 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]

DESC Plasmid pAP-197 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 293 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97900 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-190. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36881) that contains a **cleavage** site for HIV **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA and subcloning of the mutant DNA into vector pSB2. **Recombinant** baculovirus was obtained and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HIV. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97900 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-196 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 294 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97899 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-190. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36880) that contains a **cleavage** site for HIV **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA and subcloning of the mutant DNA into vector pSB2. **Recombinant** baculovirus was obtained and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HIV. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97899 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430

DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-190 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 295 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97898 DNA DGENE
AB This is the DNA sequence of baculovirus transfer vector pVL1393. A claimed baculovirus transfer vector incorporates a nucleic acid (see AAT97899-901, AAT97910, AAT97913, AAT97916 and AAT97919) that encodes a **recombinant** protein in which the A and B chains of a **ricin**-like toxin are linked by a heterologous linker peptide (see AAW36880-86) that contains a **cleavage** recognition site for a retroviral **protease** such as HIV, HTLV-I or HTLV-II. The vector provides expression of the **recombinant** proteins in Sf9 insect cells. The **recombinant** proteins can be used to selectively inhibit or destroy mammalian cells infected with a retrovirus, such as cancer cells associated with HTLV or cells associated with HIV. The **recombinant** proteins are non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells without the need for a cell binding component.
AN AAT97898 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Baculovirus transfer vector pVL1393.
IN Borgford T

L46 ANSWER 296 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97923 DNA DGENE
AB This oligonucleotide primer, designated Ricin1729C Xba, is a downstream primer of preproricin DNA and contains a 5' XbaI site. It corresponds to nucleotides 1864-1846 of the plasmid insert sequences given in AAT97899-901. Ricin1729X Xba was used with upstream primer **Ricin** -99Eco (see AAT97921) and with mutagenic primers to alter the DNA encoding the linker sequence between the A and B chains of preproricin. The invention provides novel **recombinant** proteins in which **ricin** A and B chains are separated by a heterologous linker (see AAW36880-86) which contains a **cleavage** site for a retroviral **protease** such as HIV, HTLV-I or HTLV-II. These **recombinant** proteins can be used to inhibit or destroy retrovirus-infected mammalian cells.
AN AAT97923 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Downstream primer Ricin729C Xba.
IN Borgford T

L46 ANSWER 297 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97922 DNA DGENE
AB This oligonucleotide primer, designated **ricin**-1729C, is a downstream primer of preproricin DNA. It corresponds to nucleotides 1864-1846 of the plasmid insert sequences given in AAT97899-901. **Ricin**-1729C was used with upstream primer **ricin**-109 (see AAT97920) to amplify preproricin cDNA. The amplified fragment was subsequently subjected to PCR mutagenesis to alter the DNA encoding the linker sequence between the **ricin** A and B chains. Novel **recombinant** proteins are provided in which the A and B chains are separated by a heterologous linker (see AAW36880-86) which contains a **cleavage** site for a retroviral **protease** such as HIV, HTLV-I or HTLV-II. These **recombinant** proteins can be used to inhibit or destroy retrovirus-infected mammalian cells.
AN AAT97922 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Downstream primer ricin-1729C.
IN Borgford T

L46 ANSWER 298 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97921 DNA DGENE
AB This oligonucleotide primer, designated **ricin**-99Eco, is an upstream primer of preproricin DNA and contains a 5' EcoRI site. It corresponds to nucleotides 37-59 of the plasmid insert sequences given in AAT97899-901. **Ricin**-99Eco was used with downstream primer ricin1729Xba (see AAT97923) and with mutagenic primers to alter the DNA encoding the linker sequence between the A and B chains of preproricin. The invention provides novel **recombinant** proteins in which **ricin** A and B chains are separated by a heterologous linker (see AAW36880-86) which contains a **cleavage** site for a retroviral **protease** such as HIV, HTLV-I or HTLV-II. These **recombinant** proteins can be used to inhibit or destroy retrovirus-infected mammalian cells.
AN AAT97921 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429

PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Upstream primer ricin-99Eco.
IN Borgford T

L46 ANSWER 299 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97920 DNA DGENE
AB This oligonucleotide primer, designated **ricin**-109, is an upstream primer of preproricin DNA. It corresponds to nucleotides 27-59 of the plasmid insert sequences given in AAT97899-901. **Ricin** -109 was used with downstream primer ricin1729C (see AAT97922) to amplify preproricin cDNA. The amplified fragment was subsequently subjected to PCR mutagenesis to alter the DNA encoding the linker sequence between the **ricin** A and B chains. Novel **recombinant** proteins are provided in which the A and B chains are separated by a heterologous linker (see AAW36880-86) which contains a **cleavage** site for a retroviral **protease** such as HIV, HTLV-I or HTLV-II. These **recombinant** proteins can be used to inhibit or destroy retrovirus-infected mammalian cells.
AN AAT97920 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Upstream primer ricin-109.
IN Borgford T

L46 ANSWER 300 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97919 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-212. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36886) that contains a **cleavage** site for HTLV-II **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA. **Recombinant** baculovirus was generated and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HTLV-I for the treatment of human T-cell leukaemias. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97919 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p

AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-212 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 301 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease**, used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97916 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-210. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36885) that contains a **cleavage** site for HTLV-II **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA. **Recombinant** baculovirus was generated and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HTLV-I for the treatment of human T-cell leukaemias. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97916 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease**, used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-210 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 302 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease**, used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97913 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-208. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36884) that contains a **cleavage** site for HTLV-I **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA. **Recombinant** baculovirus was generated and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HTLV-I for the treatment of human T-cell leukaemias. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97913 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease**, used to inhibit or destroy mammalian cells infected with retrovirus

IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-208 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 303 OF 306 DGENE (C) 2003 THOMSON DERWENT
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
AN AAT97910 DNA DGENE
AB This DNA sequence comprises the insert sequence of plasmid pAP-206. This plasmid was obtained by subcloning into baculovirus transfer vector pVL1393 (see AAT97898), a nucleic acid sequence encoding a protein in which the A and B chains of **ricin** are linked by a heterologous linker (see AAW36883) that contains a **cleavage** site for HTLV-I **protease**. The nucleic acid sequence was obtained by PCR mutagenesis of the linker sequence of wild-type preproricin DNA. **Recombinant** baculovirus was generated and mutant **recombinant** proricin was expressed in Sf9 insect cells. The **recombinant** protein can be used to selectively inhibit or destroy mammalian cells infected with HTLV-I for the treatment of human T-cell leukaemias. It is non-toxic until the **ricin** A chain is liberated from the B chain by the retroviral **protease**, and thus can be used to specifically target infected cells.
AN AAT97910 DNA DGENE
TI DNAs encoding **ricin** like toxins A and B - are linked via linker containing **cleavage** site for retroviral **protease** , used to inhibit or destroy mammalian cells infected with retrovirus
IN Borgford T
PA (CANG-N) CANGENE CORP.
PI WO 9741233 A1 19971106 105p
AI WO 1997-CA288 19970429
PRAI US 1996-16509 19960430
DT Patent
LA English
OS 1997-549735 [50]
DESC Plasmid pAP-206 insert encoding antiviral ricin-like protein.
IN Borgford T

L46 ANSWER 304 OF 306 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

L46 ANSWER 305 OF 306 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

L46 ANSWER 306 OF 306 ADISINSIGHT COPYRIGHT (C) 2003 Adis Data Information BV
SO Adis R&D Insight

=>